DECEMBER 1957

Drug and Cosmetic Industry

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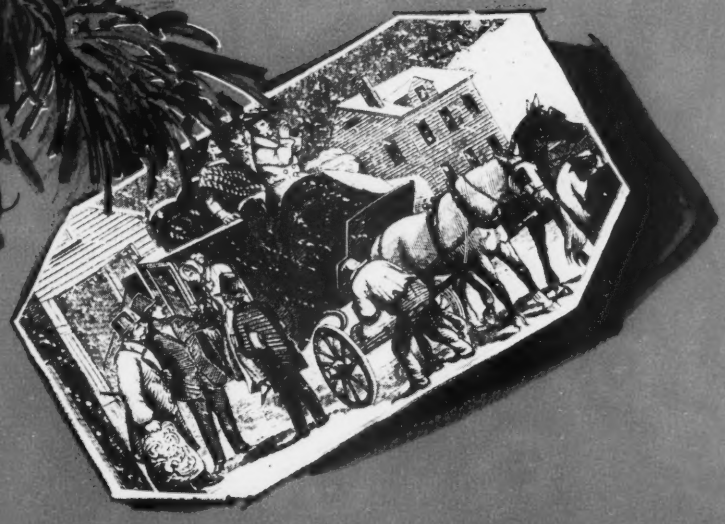

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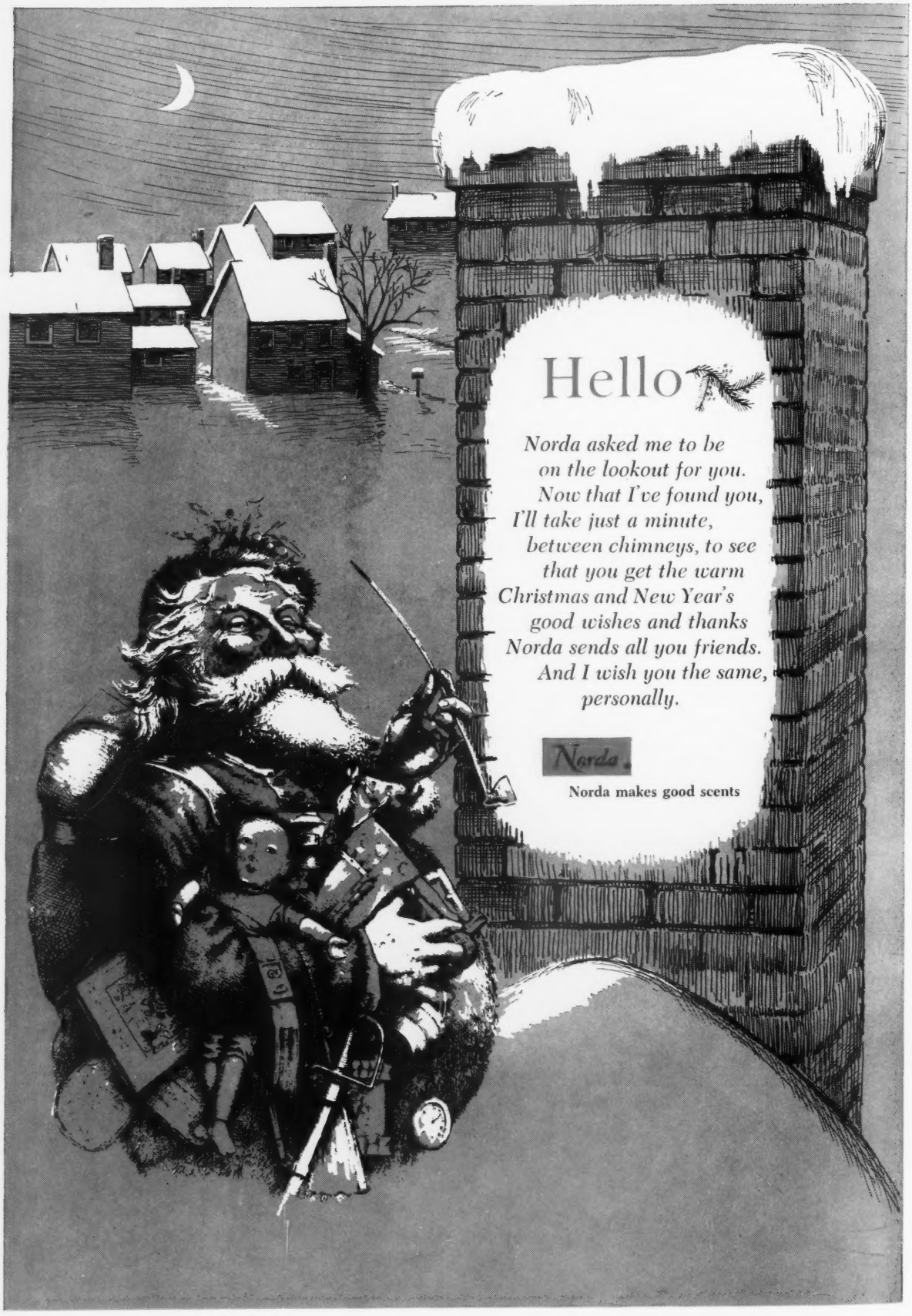
Hello
Norda asked me to be
on the lookout for you.
Now that I've found you,
I'll take just a minute,
between chimneys, to see
that you get the warm
Christmas and New Year's
good wishes and thanks
Norda sends all you friends.
And I wish you the same,
personally.
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Drug and Cosmetic Industry

Contents **December 1957 Vol. 81 No. 6**

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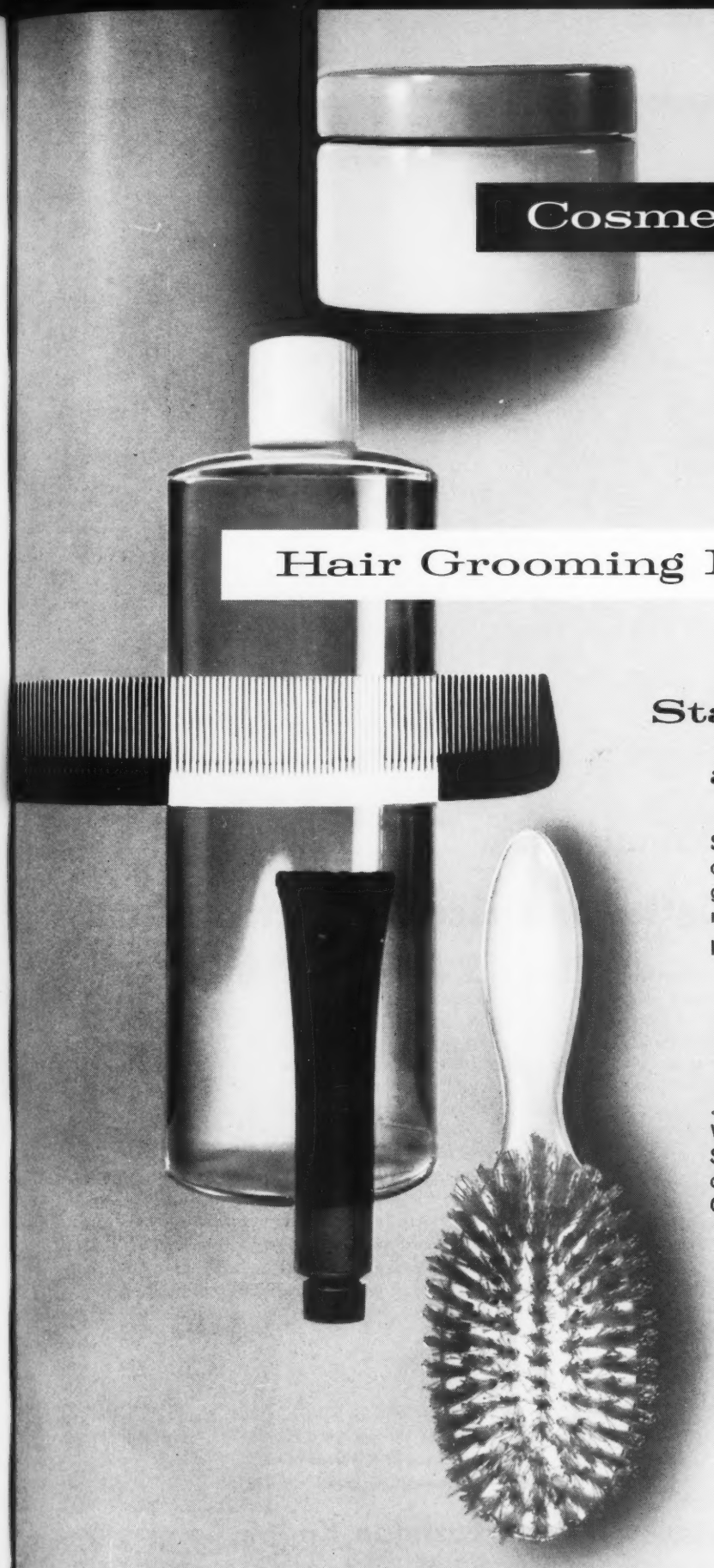

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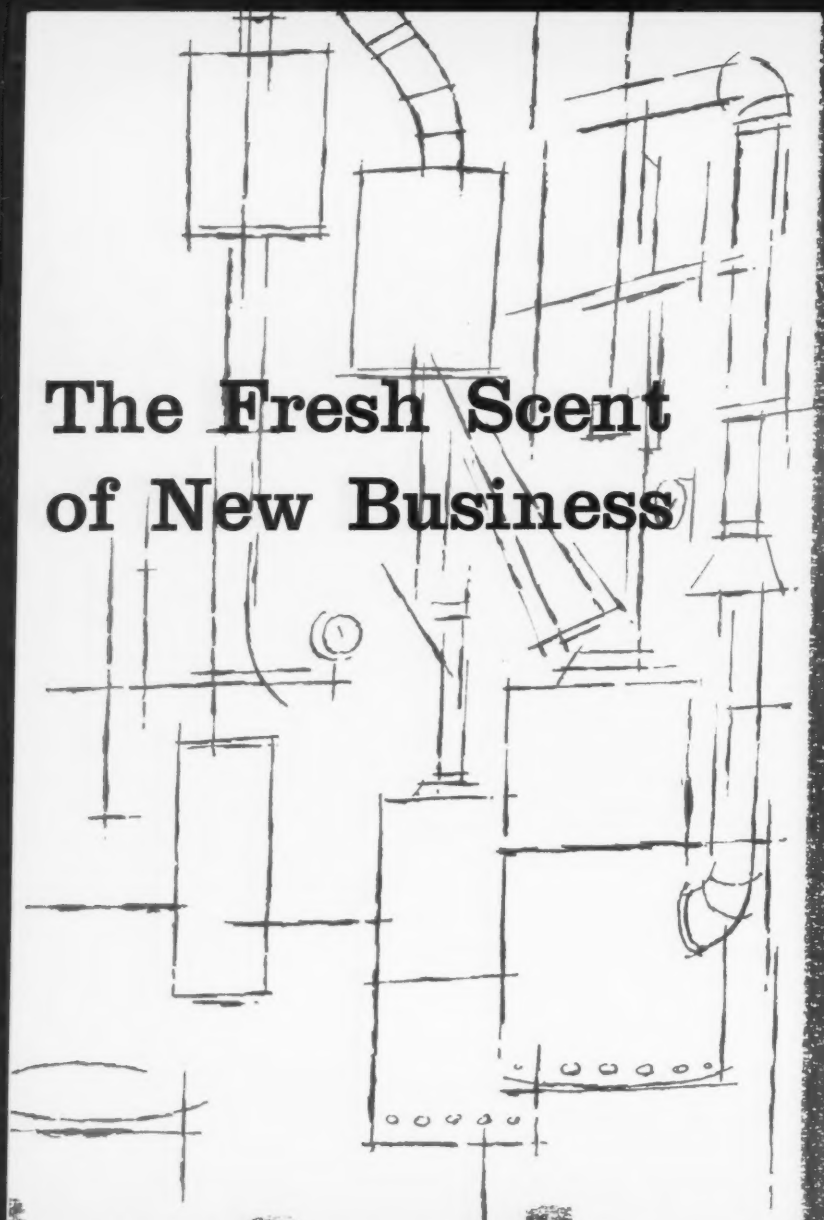

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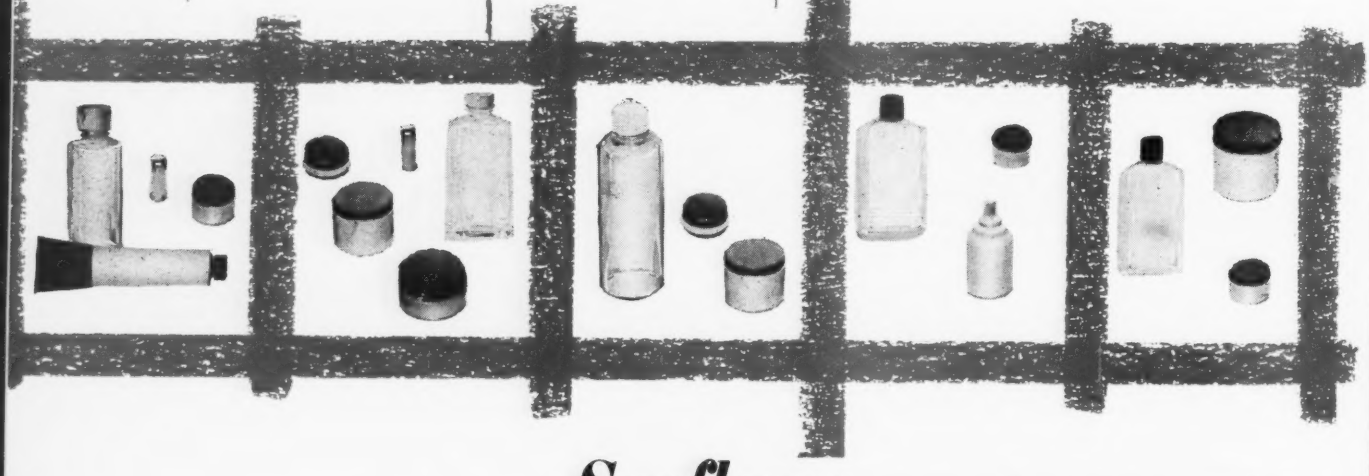

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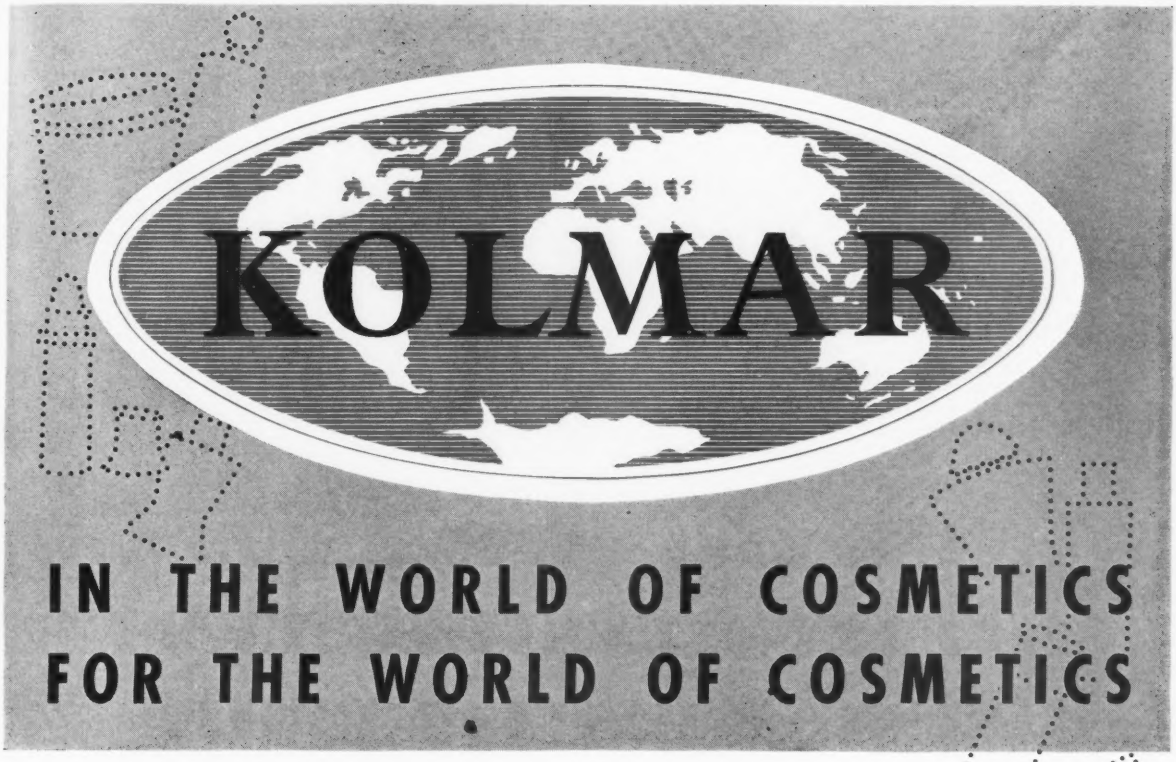

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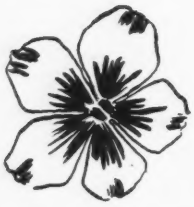

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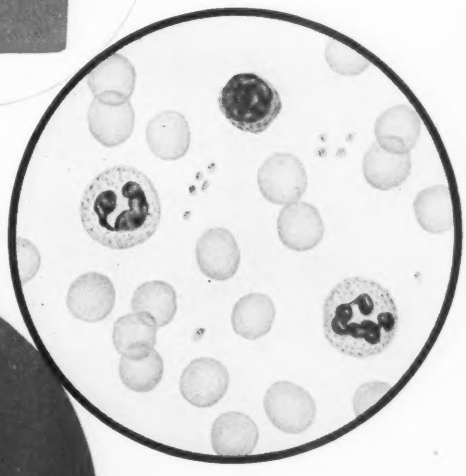

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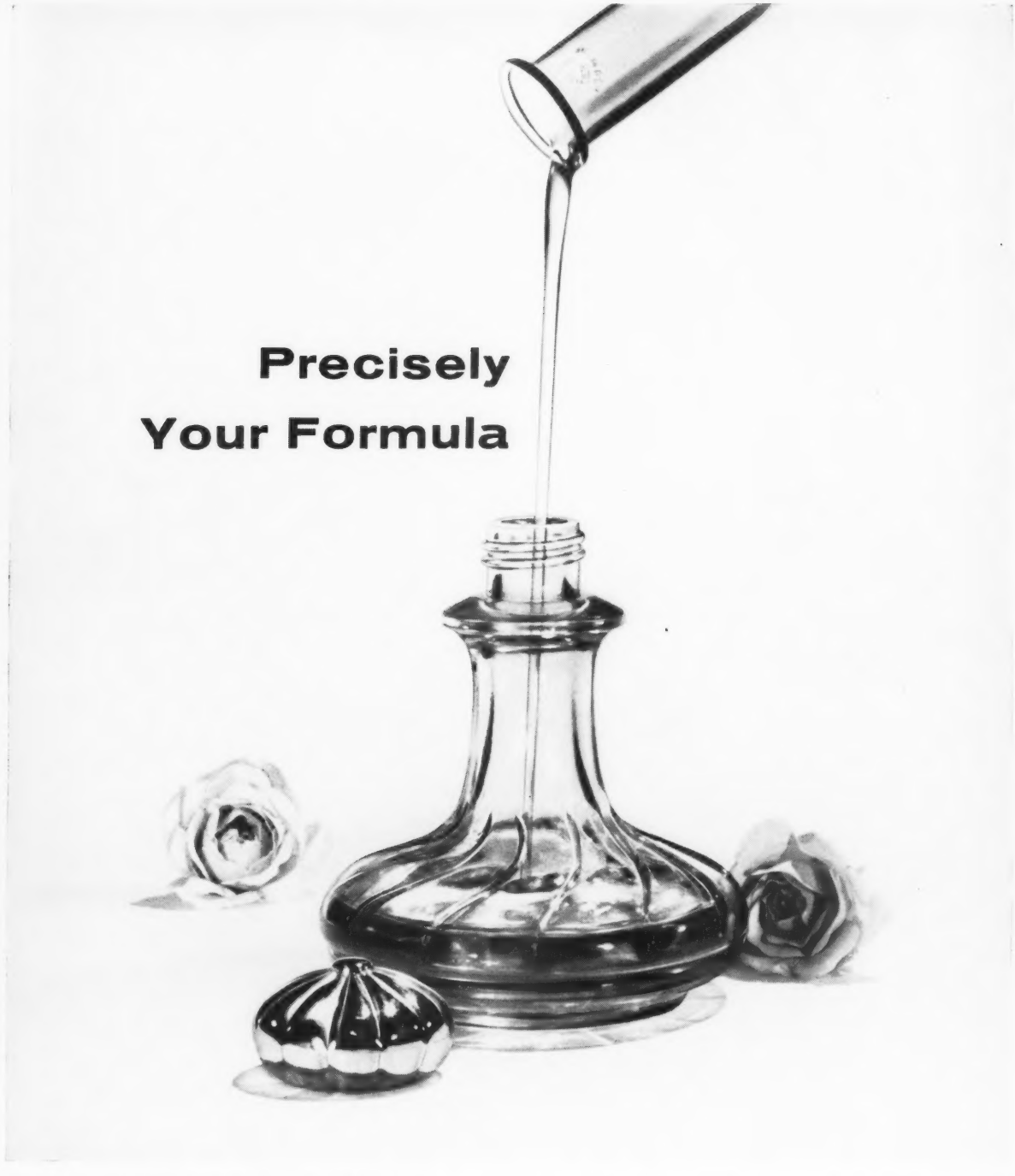

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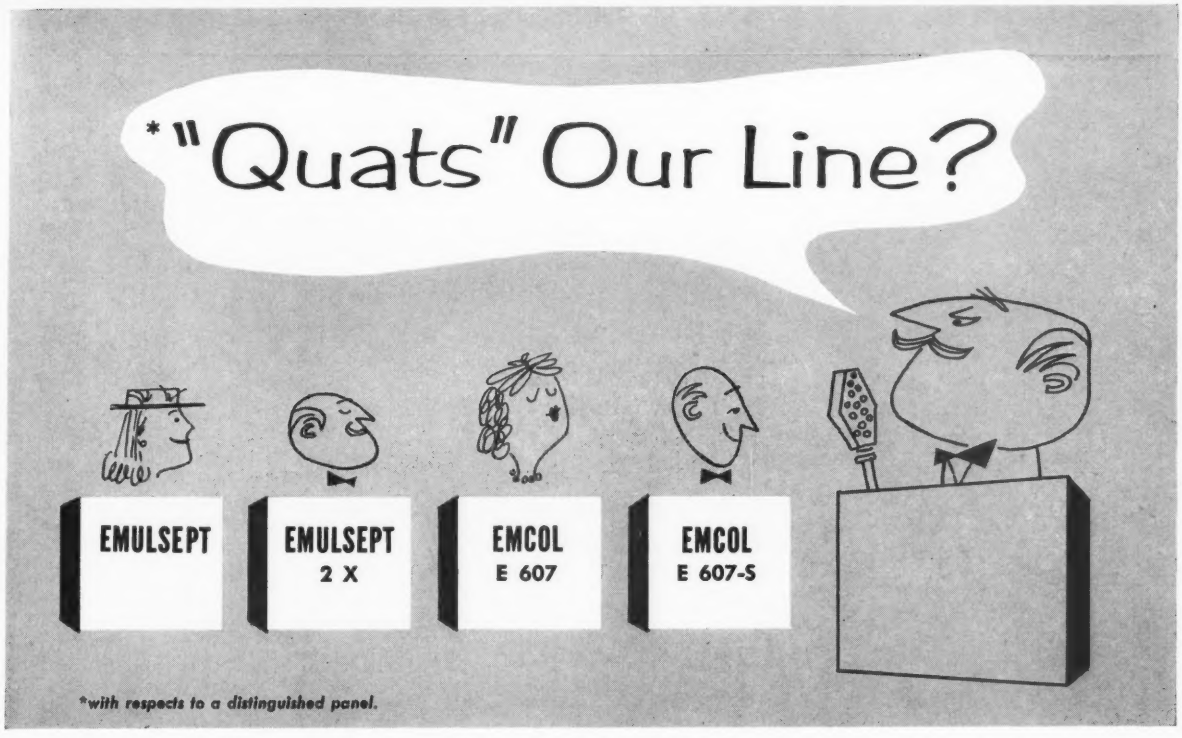

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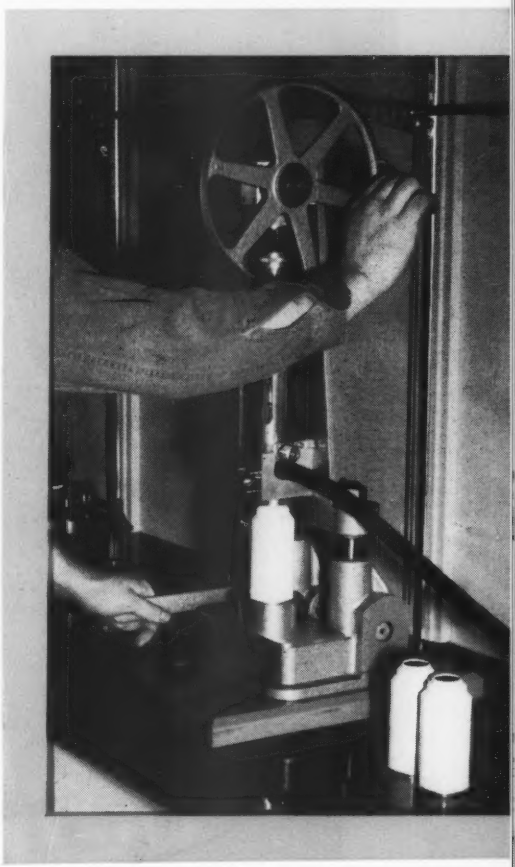

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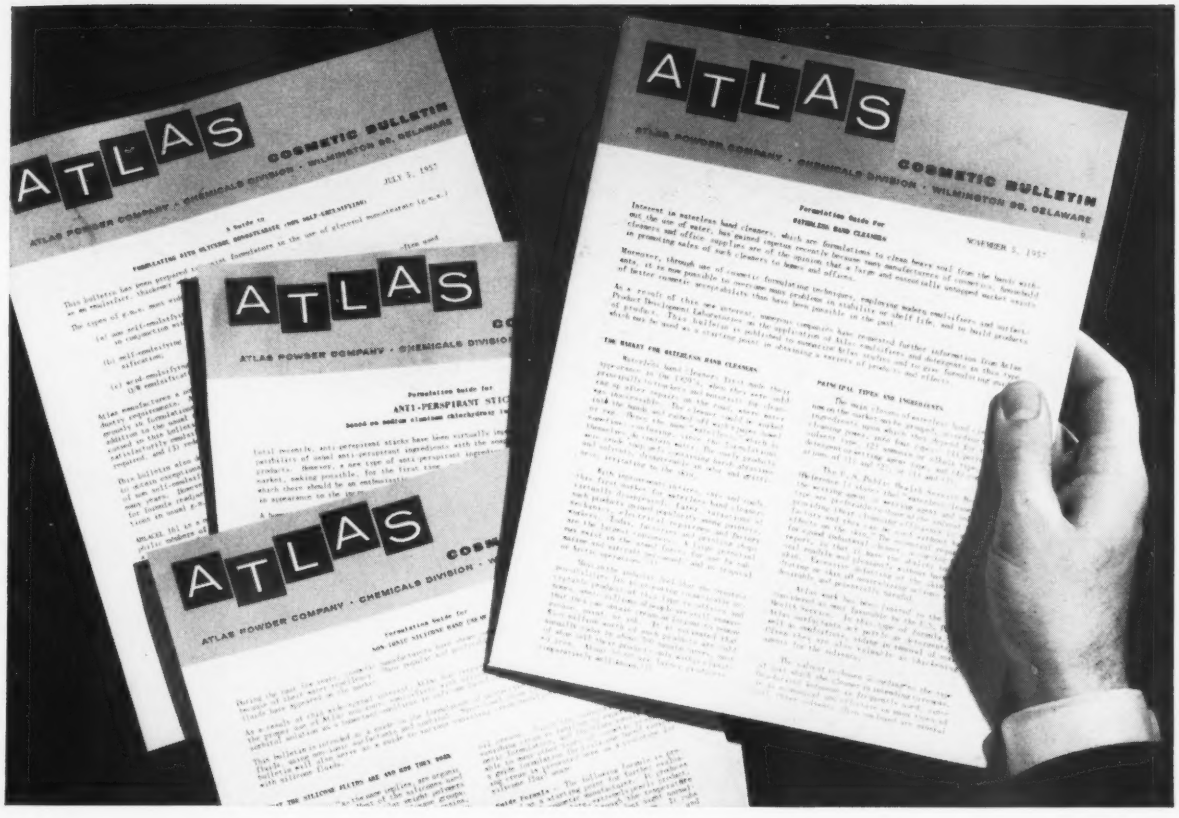
ATLAS
COSMETIC BULLETIN
ATLAS POWDER COMPANY · CHEMICALS DIVISION · WILMINGTON 99, DELAWARE
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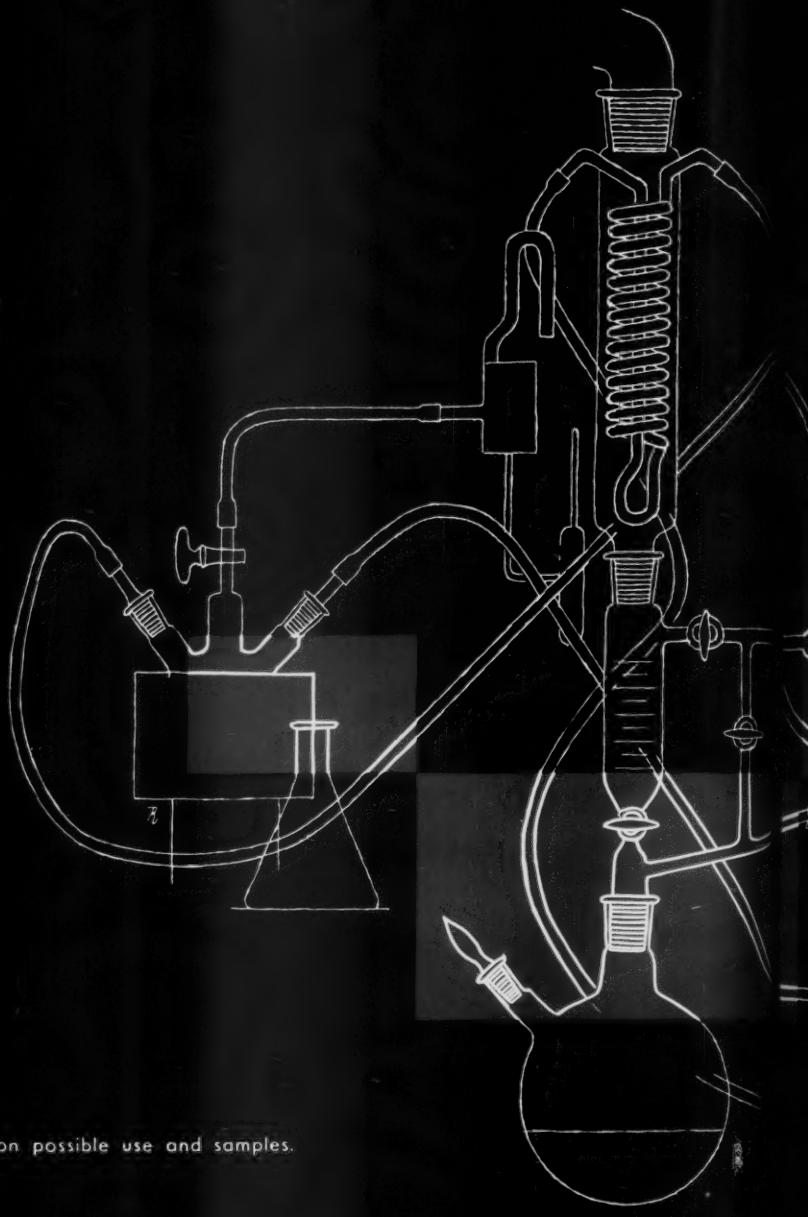
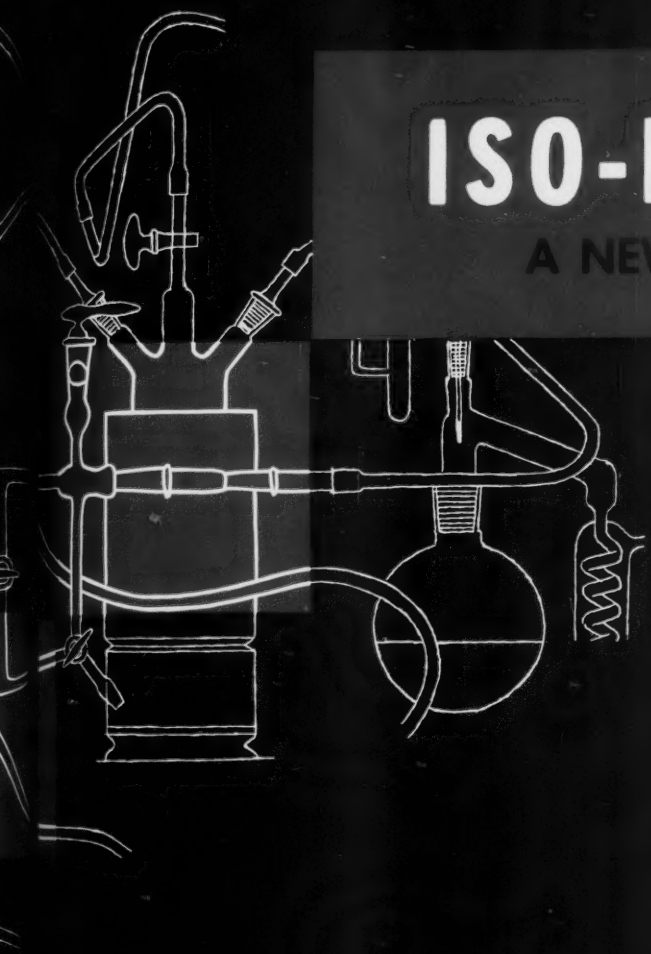


Write for chemical and physical details, information on possible use and samples.



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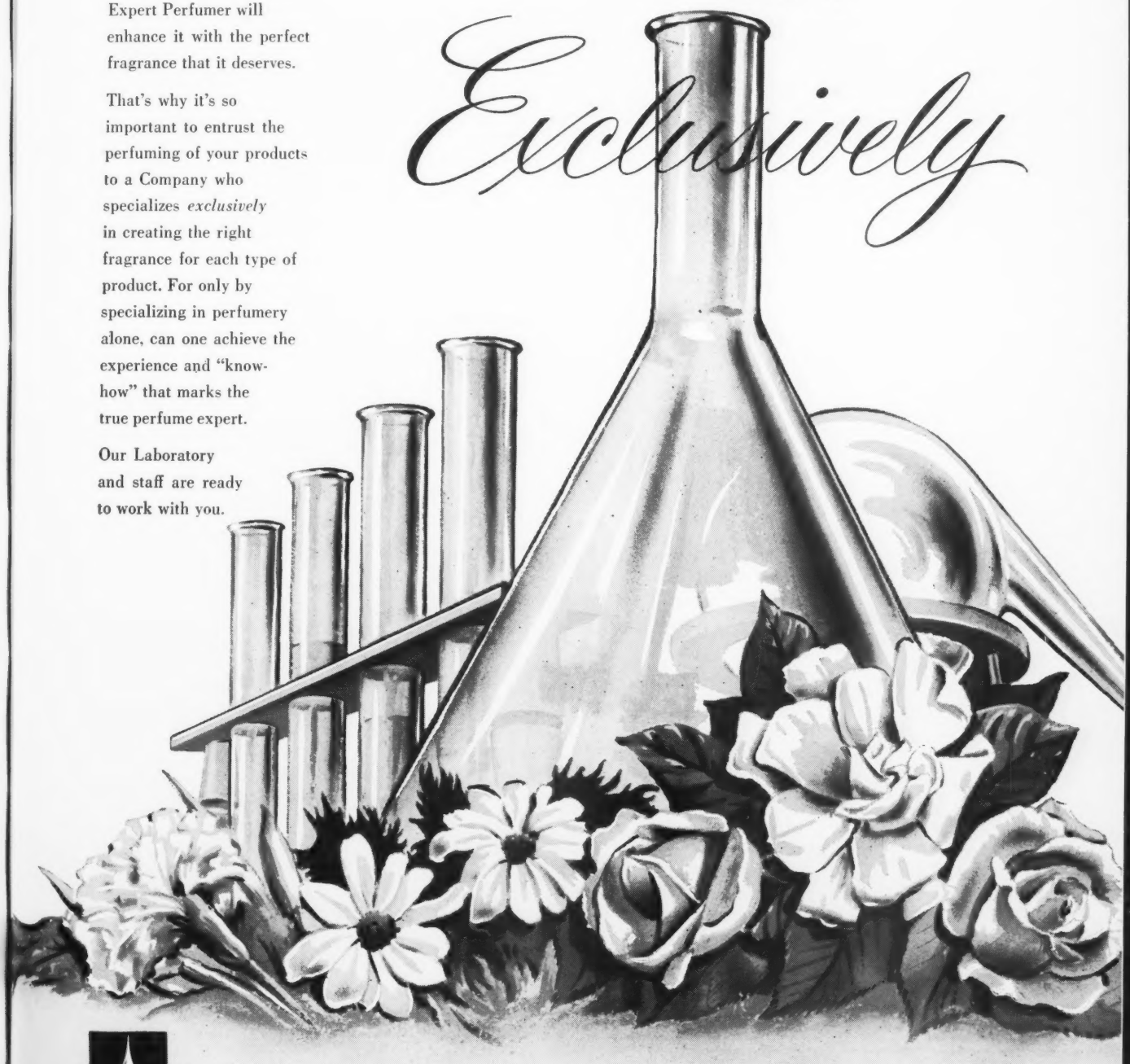

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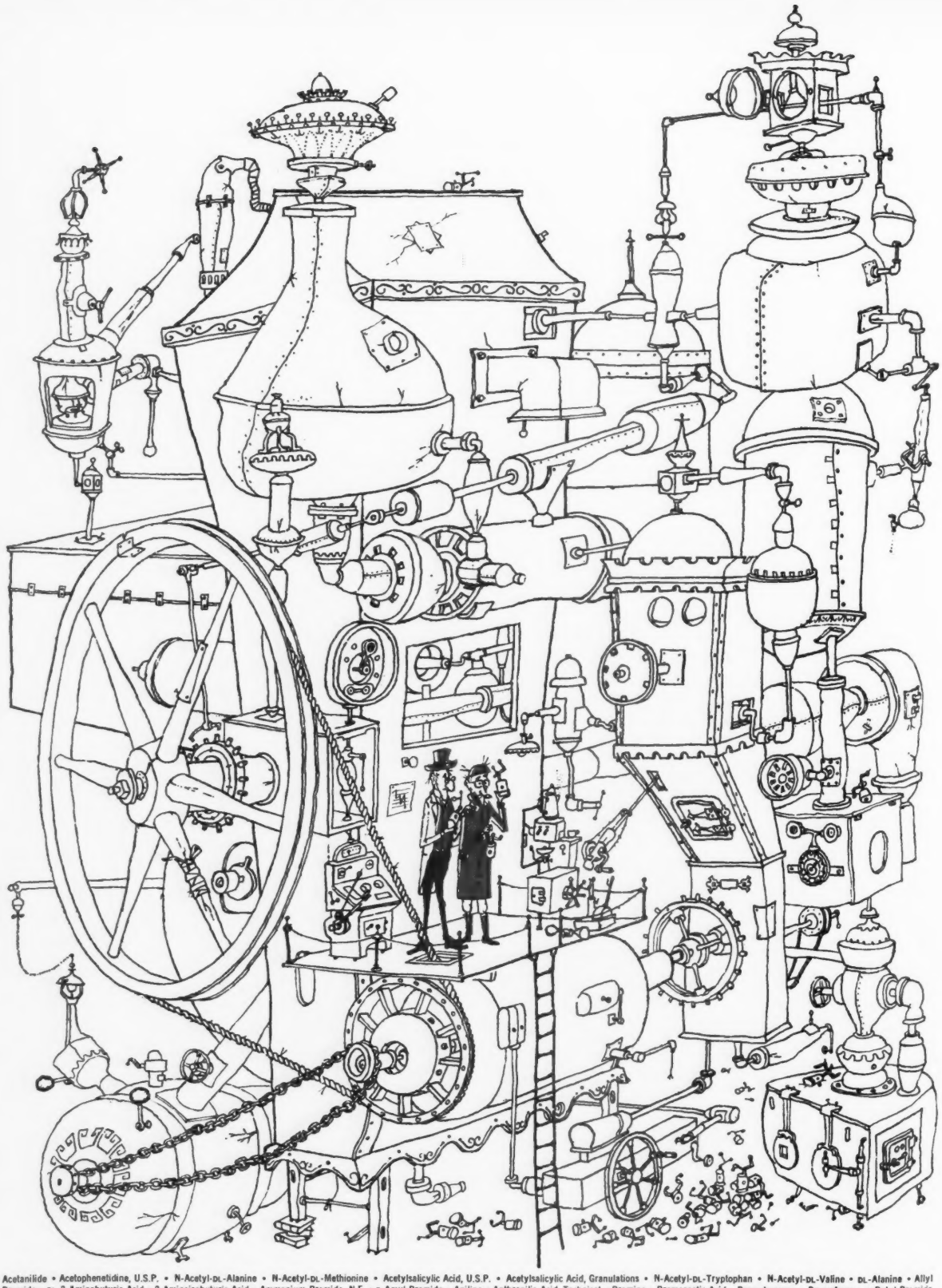

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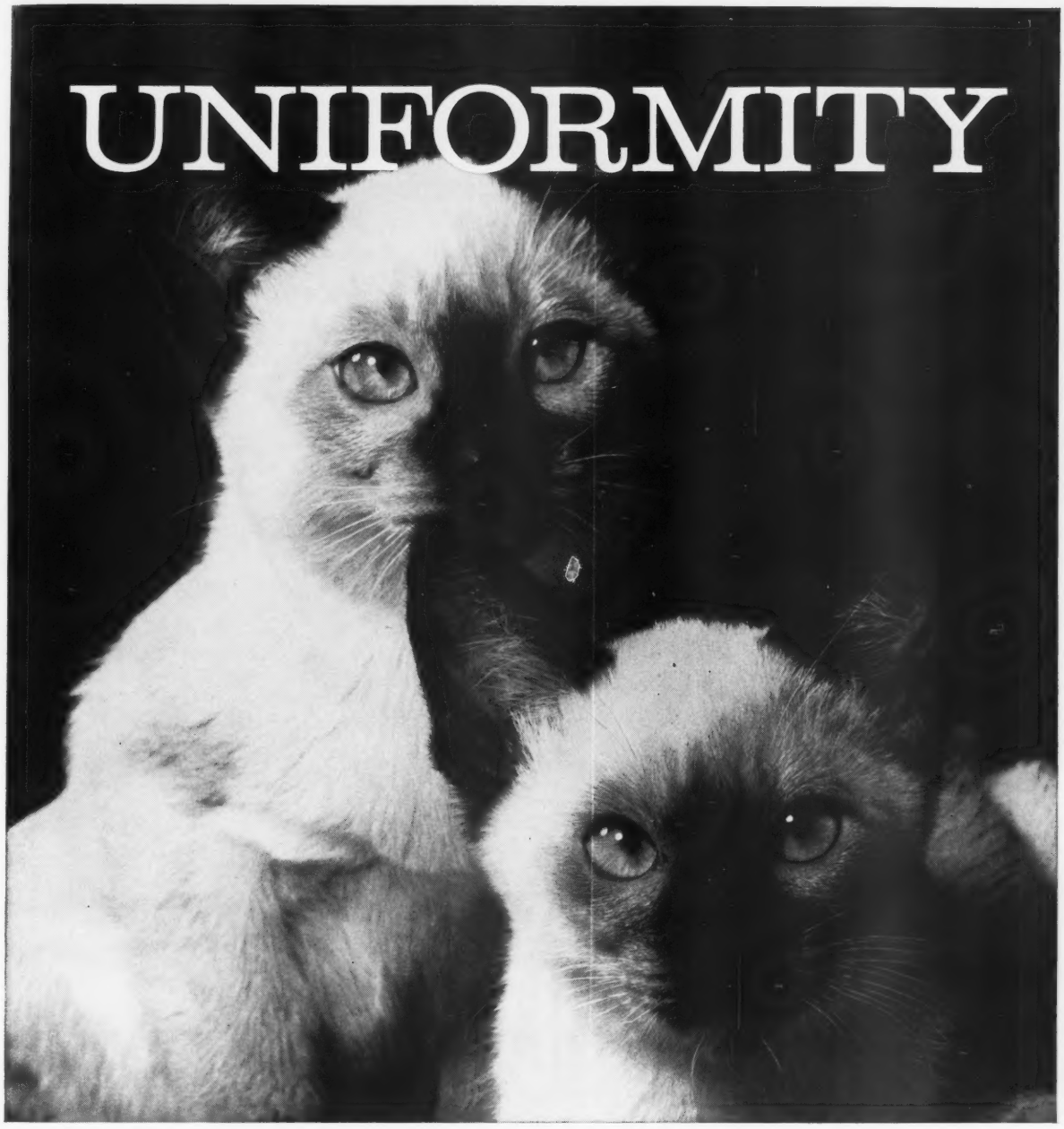

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Amyl Cinnamic
Anisic
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C 7 and C 8
C 9 and C 10
C 11 and C 12
Cinnamic
Citral
Citronellal
Cyclamic
Hexyl Cinnamic
Hydroxy-Citronellal
Iso Butyric
Phenyl Acetic
Phenyl Propylic
Piperonal
Propionic
Protobyl
Tolyl
Vanillin

PHENOLS
Anethol
Eugenol
Iso Eugenol
Iso Safrol
Methyl Eugenol
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Safrol

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ESTERS
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Anthranilate
Benzoate
Butyrate
Caprinate
Caprylate
Citrate
Formate
Heptylate
Iso Valerate
Laurate
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Manylate
Oenanthate
Oxalate
Phenyl Acetate
Phthalate
Propionate
Salicylate
Stearate
Tartarate
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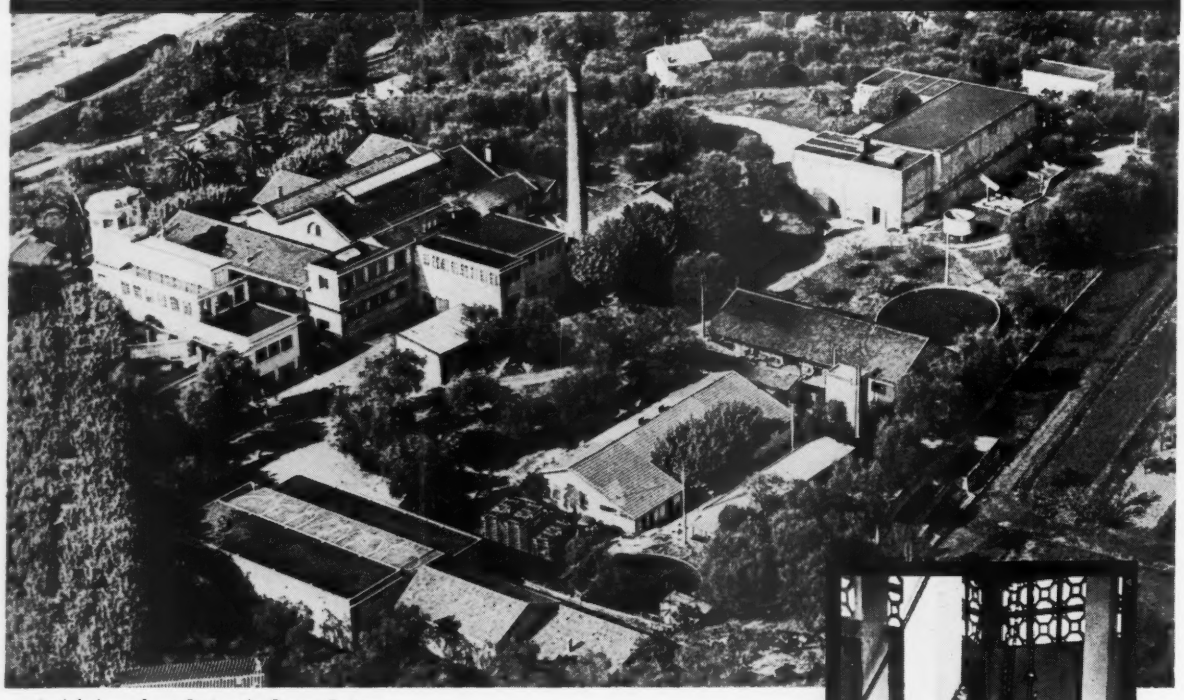

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Keeping Posted

Parke Davis Research Aims

Forty per cent of this year's research budget of Parke, Davis & Company, which averages about $6.5 million per year, went into antibiotics and synthetic chemicals research, Harry J. Loynd, Parke, Davis president, told the Detroit Financial Analysts Society. Only 200 of some 4,200 products were found active in mice, he said, and of these 200, only 30 were experimentally manufactured. Of these surviving 30, only six were clinically tested and are being considered as potential new products while further studies are made. P.D. research scientists are also active in the fields of virus-caused infections, tropical diseases, infectious diseases such as polio, cardiovascular and renal diseases, cancer, geriatrics, pediatrics, and mental health.

The greatest research advances have been made in development of vaccines to combat virus-caused diseases such as measles, respiratory illnesses, and hepatitus, said Mr. Loynd. He said one vaccine giving immunization against polio, tetanus, whooping cough, and diphtheria is being developed at P.D. He said his firm may succeed in combining a vaccine for the new Echo virus, which causes enephalitis and a paralytic disease similar to polio, with polio vaccine, "by the end of next year." During 1958, P.D. will introduce at least two new products, one a sulfa drug and the other a new product in the steroid field.

Capital expenditures for the next five years will total about $28 million, said Mr. Loynd. The "biggest share" of this amount will go toward construction of the $10 million Medical Research Center at Ann Arbor, Michigan, which will be completed and occupied by July 1, 1959. At that time the P.D. research budget will be increased to about $8 million.

Smith, Kline & French Expansion

Smith, Kline & French Laboratories has bought for $940,220, a square block containing 177,000 square feet across Sixteenth Street from their present location at 1530 Spring Garden Street, Philadelphia. Bounded on the east by Sixteenth Street, on the west by Seventeenth Street, on the north by Buttonwood Street, and on the south by the Reading Railroad right-of-way, the property was bought for future expansion. Eight of the 20 buildings on the plot will be demolished soon for utilization of the southwest corner for an employee parking lot. Other buildings will continue to be occupied by their present tenants. Purchase of the tract marks a continuation of SKF's policy to maintain its research, manufacturing, and office facilities in the center of Philadelphia.

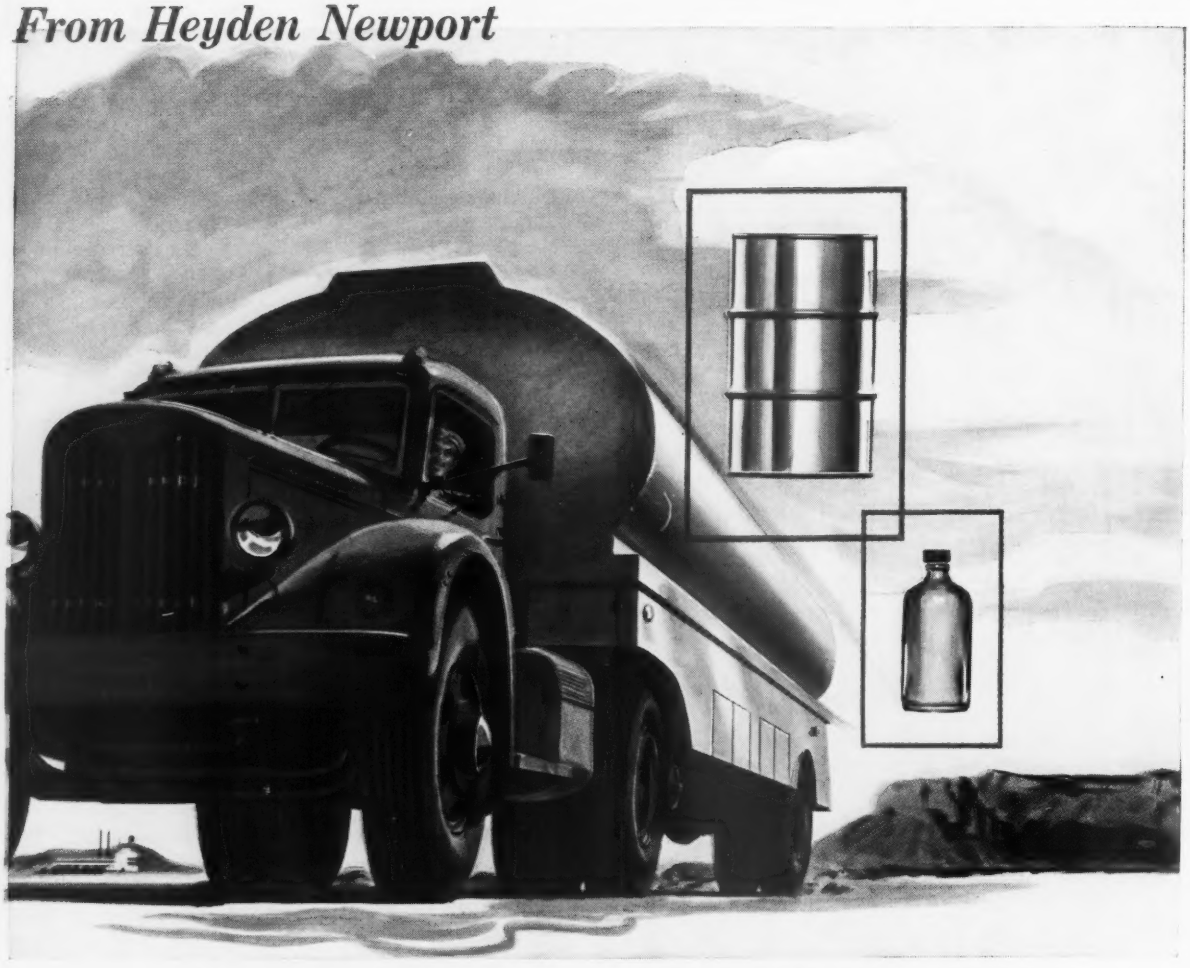
By the end of the year, SKF will have moved into a 12-story addition to the 1948 five-story plant. This will increase research, office, and manufacturing facilities from 717,000 square feet to about 858,000. SKF's only domestic expansion outside the center of Philadelphia was the purchase last year of a 25-acre tract at Gulph Mills in Upper Merion Township. A building to house laboratory animals has been completed there, and construction is proceeding on a plant to manufacture basic chemicals.

The Fair Trade Legislative Problem

As the Bureau of Education on Fair Trade lines up its forces among small business interests in retailing and wholesaling—a group which Dr. Dargavel says is "ten million strong"—to force enactment of a national price maintenance law based on the welfare of these retailers and wholesalers, the American Fair Trade Council pushes for control of resale prices through its Antimonopoly Amendment to the Lanham Act. The Council cites the decision against General Electric which authorized the sales of Masters at cut prices from Washington, D.C., to states in which valid fair trade acts exist, as the need for further urgency in having such a law enacted.

While the Bureau of Education on Fair Trade has not as yet made public its proposed measure, this bill is based on the protection of small business. However, the American Fair Trade Council bases its bill on the property rights of manufacturers in their trademarks. The Bureau of Education on Fair Trade has refused to follow the line of trademark property rights because they fear on the attacks that might be made on trademarks. Trademarks have many enemies, just as have

From Heyden Newport



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A new plant to give you high quality, readily available Salicylaldehyde will be in operation at Heyden Newport to supply your needs in 1958.

Modern plant facilities, strictest quality control, and our long experience in the manufacture of quality products will be your assurance of complete dependability with this versatile chemical.

As a reactive intermediate, Salicylaldehyde (o-hydroxybenzaldehyde) has found extensive use in the preparation of coumarin, pharmaceuticals, dyestuffs, and additives for the rubber and petroleum industries. Salicylaldehyde likewise serves the essential oil and plating industries.

Let Heyden Newport fill your requirements for Salicylaldehyde—your products and processes will benefit from quality protection and assurance of adequate supply.

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patents, and manufacturers do not wish to give these enemies any ammunition with which to launch a new attack on trademarks.

The American Fair Trade Council bill, which is available, gives the owners of trademarks the right to revoke a price-cutter's use of a trademark anywhere. The owner of the trademark then buys back the price-cutter's stock of his goods, or permits the retailer to conduct a good-faith close out sale for a reasonable time. After that, any use by the price-cutter of that trademark would put the price-cutter in violation of the Lanham Act and would subject him to the same severe penalties as a counterfeiter of a registered mark.

TGA Extends Ad Service to Non-Members

The Board of Standards on advertising copy review of the Toilet Goods Association, which in the past has made its services available only to TGA members, has extended its services to any member of the industry who wishes to take advantage of them. The TGA, through S. L. Mayham, executive vice-president of the association, points out that the Board of Standards, established nearly twenty years ago, has a "completely perfect record with respect to the actionability of copy and labeling statements." In other words, "No piece of copy, either labeling or advertising, which has been approved by the TGA Board of Standards, has ever been made the subject of a case by either the Food and Drug Administration or the Federal Trade Commission."

This extension of these services by the TGA to non-members is due to the association's feeling that "the growth of borderline, or even directly misleading, advertising on the part of certain members of the industry" over the last few years calls for a policy of "self-policing" before Congressional thinking on the subject results in seriously objectionable laws being proposed or enacted.

The board and its operation are described as follows: "The Board of Standards of the TGA consists of the executive vice-president of the association, the scientific director of the association, and the general counsel of the association. No manufacturer (competitor) is a member of the board or takes any part in this activity. No manufacturer, whether a member or not, has access to the copy file of the Board of Standards, and no request for information from any manufacturer, large or small, with respect to the advertising claims or copy of another manufacturer has ever been or ever will be answered. The board does not even tell one manufacturer whether another manufacturer is submitting his copy or not. In short, the entire procedure of the Board of Standards is completely secret and is kept religiously so in the interest of fairness to all.

"The way this works is as follows: The manufacturer submits to the Board of Standards of the Toilet Goods Association, in duplicate, any proposed piece of copy in advance of its publication. The board returns one copy of it and preserves one copy, with an official stamp which says one of three things: (A) Approved; (B) Approved with Corrections; (C) Not Acceptable."

The address of the TGA is 1270 Avenue of the Americas, New York 20.

Merck Policies

The importance which Merck & Co. attaches to its Chemical Division product line modernization program is indicated by the fact that the Chemical Division will account for better than half of the company's capital expenditures for 1957, Merck President John T. Connor recently told the Boston Security Analysts Society. Mr. Connor also pointed out that before the merger of Merck and Sharp & Dohme, the latter company had almost 600 products in its line, the majority of which were open formula competitive items. Mr. Connor continued:

"Another group such as Sucrets and S.T. 37 were drugstore merchandising items, while only comparatively few of its products were prescription specialties requiring extensive detailing of physicians. Things are different now. The large majority of its important products are prescribed specialties, such as Co-Deltra, Meprolone, Cathomycin, and Inversine, which require the understanding and cooperation of the physician. The entire direction of our sales effort has been changed to reflect that need. The merchandising items are still important components of our line, and we continue to promote them through the druggists.

"Now completely absent from the line are literally hundreds of drug products readily available from other sources, and in which our Company had no particular position. The effect has been to enable our sales representatives to concentrate on our more important products during the short time they have in the offices of the always busy specialists and other doctors.

"Therefore, in analyzing our recent operating reports, you should be aware of the fact that we are going through a production deletion program that is eliminating some millions of dollars from the sales line that otherwise would be there. The beneficial results of concentrating our efforts on the more important products are already becoming apparent. I'm sure you've noticed that we've been able to increase our profit margin somewhat even in a period of rapidly rising costs and uncertain and declining prices."

Downs Flouridation

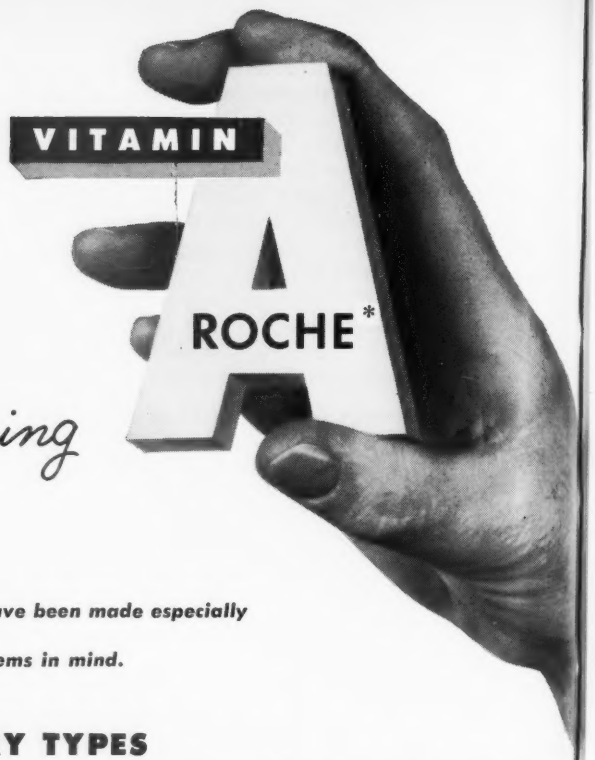
Despite the fact that a committee of the World Health Organization, and the American Dental Association, and other scientific bodies have endorsed fluoridation of water supplies for the protection of children's teeth against decay, Dover, New Hampshire defeated a proposal for fluoridation of the city water supplies by a vote of 3,949 to 668. Two members of the Board of Health campaigned vigorously against the plan claiming that fluorides are poison, especially harmful to elderly people, and that their use is advocated by Communists. The Dover Dental Society and several parent-teacher groups supported the proposal.

Celeste Holm and the AFPE

Having recently scanned the list of close to two hundred 1957 patrons of the American Foundation for Pharmaceutical Education, we came across a name that seemed out of place among all the various drug, cosmetic, and other companies affiliated with the drug industry. The name was Celeste Holm, the well known actress and entertainer. We immediately inquired from Paul Briggs, executive director of the AFPE as to

Memo to: executives, purchasing agents, technical people

Roche has all popular types of Vitamin A for your pharmaceutical manufacturing



Take your choice of the following types of vitamin A Roche. These have been made especially with your various manufacturing and compounding problems in mind.

IQUID TYPES

ype P1MO vitamin A palmitate—1,000,000 U.S.P. units per gram, standrdized by addition of edible vegetable oil. This type is a highly refined roduct containing well-proven stabilizing factors of the Roche synthesis. *xperience has shown that this type meets the great majority of pharıaceutical requirements.*

ype P1MO/BHA vitamin A palmitate—Same as Type P1MO above plus ıe antioxidant-butylated hydroxyanisole (10 mg. per 1,000,000 units of itamin A).

ype A1MO vitamin A acetate—1,000,000 U.S.P. units per gram, standrdized by addition of edible oil. Contains well-proven stabilizing factors f the Roche synthesis.

ype P1.3 vitamin A palmitate—ranging between 1,350,000 and 650,000 U.S.P. units per gram. Does not contain any oil addition. leally suited for oil-free preparations. Stability is similar to type P1MO.

SPECIAL TYPES

ype P1.8 vitamin A palmitate—1.65 to 1.8 million U.S.P. units per gram.

ype A2.9 vitamin A acetate—2.8 to 2.9 million U.S.P. units per gram.

hese special types are available for research and special production in hich special handling can be provided.

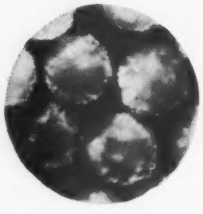
•

ackaging—All liquid types of Roche vitamin A are packed under inert as in seamless containers. Nominal quantities are shipped in wideıouth aluminum bottles. For large orders, a specially-designed aluminum transport can holding 50 kilos is recommended. A dispensing attachent is available.

amples on request; ask your Roche salesman or write Vitamin Division.

DRY TYPES

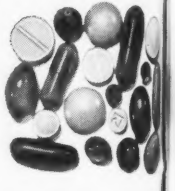
Roche dry vitamin A acetate, and vitamin A and D_2, powders have gr advantages.



First, extrusion loss is low. This advantage com from the product's excellent resistance to t high pressures found in tablet making.

Second, having an irregular surface the Roc product does not separate from other dry ingr dients during mixing or vibrating.

Third, Roche powders do not stick to machine dies and punches. Capping and spring do not occur during compression.



Fourth, dry vitamin A acetate Roche has high stability in tablets, hard and soft gelatin capsules and powdered food supplements.

The following Roche types have been found most popular:

Type 500-dry vitamin A acetate. 500,000 U.S.P. units per gram.

Type 325-dry vitamin A acetate. 325,000 U.S.P. units per gram.

Type 500 A-50D-dry vitamin A acetate and vitamin D_2. 500,000 U.S.P. units of vitamin A and 50,000 U.S.P. units of vitamin D_2 per gram.

Mesh Sizes: Each type available in two mesh sizes: No. 40 and No. 6

Packaging. All types of Roche dry vitamin A are packed in polyethylene bags, with protective sealer, in drums and in 1 and 2 kilo tamperpruf metal containers. Small quantities in amber screw-cap bottles.

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why her name was on the list. This is what Paul had to say:

"Briefly, Herman Nolen seized on Miss Holm's suggestion that her fee from McKesson for a performance at the A. Ph. A. meeting be donated to a worthwhile organization in pharmacy. Herman proposed that her gift be made to AFPE and she very graciously followed his suggestion. This is all there is to the story, except that it would be a very nice precedent for other high salaried, high tax bracket entertainers who perform before meetings of the drug industry. Any suggestions as to an approach for this new support to AFPE?"

Proprietary Association and Drug Claims

The Proprietary Association points to what has been accomplished through its service to members on a voluntary basis to aid its members in writing sound labeling and advertising of member companies' products. Frederick J. Cullen, M.D., who from 1934 to 1956 was executive vice-president and is now medical consultant to the Association, has for twenty-three years offered expert review of labeling and advertising copy. As to the value of this service, the Association cites the results of a recent survey of all Federal Trade Commission complaints against manufacturers of proprietary medicines for claims made in advertising. During the period January 1, 1950 to October 31, 1957, the Commission brought complaints against the manufacturers of forty-five proprietary medicines, only six of which were against members of the Association.

With respect to labeling of drugs and medicines, the same survey showed more impressive results. During the period January 1, 1950 to May 31, 1957, the Food and Drug Administration brought actions against 283 proprietary medicines. Only four of the products proceeded against by the FDA were made by members of the Association.

Dr. Cullen has reviewed and returned written comment to members for over 55,000 pieces of advertising copy and several hundred label statements during the last five years, it is stated.

Prescriptions and Specialties

Fifteen leading companies shared 139,295, or 71 per cent of 195,959 of specialties in a prescription survey made during 1956 with the cooperation of Abbott Laboratories and many U.S. pharmacy colleges. These companies are: Abbott, Burroughs-Wellcome, Ciba, Hoffmann-La Roche, Lederle, Lilly, Merck-Sharp & Dohme, Parke Davis, Pfizer, Robins, Schering, Smith Kline & French, Squibb, Upjohn and Wyeth.

Of a total of 219,830 prescriptions surveyed, 191,064, or 87 per cent, contained one or more specialties—the total number of specialties used in these prescriptions totaling 195,959 of a total of 243,286 ingredients. U.S.P. ingredients, including non-trade name penicillins, totaled 40,221; N.F. ingredients, 2,275, and others, 4,831.

Prescriptions dispensed as manufactured totaled 206,309, or 94 per cent, while prescriptions requiring compounding totaled 13,521, or 6 per cent. A manufacturer's name appeared on 41,875 prescriptions. Competitive products appeared 47,327 times with no brand specified. The number of different products in the prescriptions was 3,313. The number of products appearing one or more times per 1,000 prescriptions was 229. The total selling price of the prescriptions was $534,250.26.

Prices for 14.3 per cent of the prescriptions were under $1.00; 37.4 per cent were priced from $1 to $2; 19.7 per cent from $2 to $3; 10.9 per cent from $3 to $4; 7.7 per cent from $4 to $5; 4.5 per cent from $5 to $6; 4.8 per cent from $6 to $10; and 0.7 per cent above $10.

Bristol-Myers Buying Grove

Bristol-Myers Company is purchasing Grove Laboratories, the merger to take place early in January, 1958. Founded as the Paris Medicine Company in Paris, Tennessee by Edwin Wiley Grove Sr., the company marketed its first product, Grove's Tasteless Chill Tonic in 1878. This quinine suspension is still sold in few Southern areas. Two years after the company was moved to St. Louis in 1891, Bromo Quinine Cold Tablets were developed. Pazo Ointment for hemorrhoids, was acquired in 1899. In July 1934, the name was changed to the Grove Laboratories. The founder served as president until his death in 1927, being succeeded by Edwin W. Grove Jr., who served until 1931. F. U. Hammett, John R. Shepley, and H. B. Goldsmith were successively presidents from 1931 to 1946 when James H. Grove, grandson of the founder, took over to serve as president to the present time.

In 1935, the company developed 4-Way Cold Tablets, which became the largest selling cold tablet, unitwise in this country. Grove bought the assets of The F. W. Fitch Company, makers of shampoos, cosmetics and barber supplies, in 1949, and in the same year agreed to make and distribute Pfunder's Tablets for hyperacid stomachs for the Pfunder estate. A new cold preparation, Citroid Compound, was launched by the Clayton Laboratories Division of Grove in 18 major cities in 1955, and nationally in 1956. Also in 1956, Grove bought Harrison Products, maker of NoDoz Tablets.

Monopoly Charged in Steroid Hormones

The government has brought antitrust action against four affiliated companies engaged in the steroid hormone business. The companies are Ogden Corporation and Chemical Specialties Co., both of New York, Syntex S.A., of Mexico, and American Steroid, Inc., of Puerto Rico. It will be recalled that Ogden Corporation was the purchaser of Syntex S.A. of Mexico, and that Chemical Specialties Co. was always the outlet for the products of Syntex in this country. American Steroid is also an affiliated company.

The charge is that these companies have conspired and combined to monopolize hormone imports into this country. Synthetic steroids and their intermediates are made from barbasco root which grows wild and in abundance in Mexico. Barbasco roots and its derivatives are said to be economical, efficient, and flexible starting materials for production of synthetic hormones. The hormones are used to make cortisone, hydrocortisone, prednisone and similar drugs.

The Justice Department charges that the defendants: Prevented other manufacturers from obtaining a source of barbasco root; entered into restrictive agreements with other manufacturers to control supplies of

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hormones in this country; sought to coerce competitors to limit their production and to join in price-fixing and customer allocation agreements; sold to competitors' customers at unusually low prices to deprive these rivals of business; imposed restraints on the use after sale of their products to customers to eliminate them as possible competitors; threatened and engaged in harassing patent litigation to maintain control over the industry; acquired control of the industry through predatory practices.

Dr. George Rosenkranz, chairman of the board of Syntex S.A., said:

"It appears that the Justice Department alleges principally that former activities in Mexico, by a Mexican corporation then owned solely by Mexican stockholders, which were fully in accord with Mexican law, have violated the antitrust laws of the United States. Syntex S.A. and its related companies have never willfully violated the law . . . . Syntex was acquired from its former Mexican stockholders by Ogden Corporation last year. Following the acquisition, Ogden publically announced a policy of complete compliance with the United States antitrust laws, which we have attempted to follow in all respects."

More False Advertising

Public confidence in drug and cosmetic advertising is seriously threatened because of some promoters who are making false or misleading claims to sell so-called treatments which are often worthless, and, in some cases, potentially dangerous for many users, says the National Better Business Bureau. For the past year or so, the number and flamboyancy of these advertisements have been increasing at an alarming rate, says the Bureau, which reports it is receiving four times as many inquiries concerning advertising of drugs and cosmetics as it was two years ago—and ten times as many complaints.

Cited as a particularly dangerous situation is the mail order sale of certain types of proprietaries. The Bureau says it has detected a definite pattern in the spread of bad advertising in this field. Following the introduction of an obesity remedy extensively advertised with claims backed by psuedo-scientific research, there are, within an incredibly short time, numerous imitators using the same phony evidence to support progressively extravagant claims. Then a few months later, someone introduces a new reducing "discovery" and the entire process is repeated.

To Develop Clinical Investigators

The Medical Section of the American Drug Manufacturers Association has established a fellowship for training in clinical investigation under the direction of Louis C. Lasagna, M.D., associate professor of medicine at Johns Hopkins. The ADMA Medical section—composed of medical directors of member companies—is vitally interested in early and accurate appraisal of the utility and safety of new drugs. A subcommittee on Medical Manpower, under the chairmanship of I. C. Winter, M.D., of G. D. Searle & Co., has been concerned about the lack of specially trained clinical investigators with adequate facilities to make and interpret such studies.

The fellowship is an experiment. Established for a two-year period at $7,500 per year, the actual duration and expense of such training must be confirmed by experience. It is hoped that this program will act as a "seeding" operation in that individuals so trained may establish similar departments in other educational institutions, so that the adequate training of appreciable numbers of individuals qualified to conduct clinical investigations will be achieved.

It is felt that individuals so trained should prove to be not only able investigators in their own right but better educators and clinicians as well. It is also hoped that eventually a more adequate supply of suitably trained individuals will be available for employment in the medical departments of the pharmaceutical industry since it follows that the employment of individuals with sound training and critical judgment will do much to raise the standard of new drug evaluation in this country.

The physician selected by Lasagna for the first fellowship is Dr. William P. McCann, a Princeton graduate who obtained his medical degree at Cornell, interned in St. Louis, had postgraduate training in pharmacology and physiological chemistry, and for the past two years carried on research in the Division of Clinical Pharmacology, at Johns Hopkins.

O'Connor Supports Basic Research

Basil O'Connor, president of the National Foundation for Infantile Paralysis says that the public is ready to support basic research "unconnected with a magic name like polio or cancer or heart disease. He said that the Foundation hopes to add the better part of $1 million to basic research next year, thus raising the Foundation's need for research funds to $4.7 million for 1958. The greater part of the $44.9 million the organization is seeking will be allocated for care and rehabilitation of polio victims.

Mr. O'Connor explains that the Foundation has always carried on a large program of basic research, which "has already led to the Salk vaccine." The development of a successful vacicne against polio by Dr. Salk was made possible, said Mr. O'Connor by earlier basic research, "notably the discovery by National Foundation grantee Dr. John Enders and his associates in Boston that polio viruses could be grown easily in great quantities in cultures of non-nervous tissue in laboratory bottles and test tubes." For this accomplishment Dr. Enders was awarded the Nobel Prize.

Among projects the Foundation plans to continue and expand are studies of virus structure and behavior, studies of the structure and function of nucleic acid and research into the properties of cells that appear to have become malignant while being grown in laboratories.

Lasker Awards

Six pioneers in the use of tranquilizers in mental disorders received the annual Albert Lasker Awards of the American Public Health Association in New York last month. They are: Dr. Rustom Jal Vakil, King Edward Memorial Hospital, Bombay, India; Dr. Nathan S. Kline, director of research, Rockland State Hospital, Orangeberg, New York; Dr. Robert H. Noce, Modesto State Hospital, California; Dr. Henri

Laborit, Hospital du Val de Grace, Paris, France; Dr. Pierre Deniker, former chief of clinic, medical faculty, Psychiatric Hospitals, Paris; and Dr. Heinz E. Lehmann, clinical director, Protestant Hospital, Montreal, Canada.

Others receiving the awards are: Dr. Richard E. Shope, Rockefeller Institute for Medical Research, New York, for work against infectious disease; Dr. Frank C. Boudreau, director, Milbank Memorial Fund, New York, for promotion of better health and welfare; and Dr. C. J. Van Slyke, associate director, National Institutes of Health, Bethesda, Md., for contributions to public health through medical research and scientific training.

P. & G. Answers F.T.C.

In answering the FTC complaint issued against Procter & Gamble because of P. & G.'s purchase of The Chlorox Company, P. & G. claims that technological advances and changes in consumer preference for products will influence sales substantially more than change of ownership of the company making them.

While the company admits giving away 30 million miniature "Comet" samples at a cost of $3.3 million or more, it denies "for lack of knowledge and information" that this household cleanser has captured 29 per cent of the market as claimed by the Commission. The company also points out that it has sometimes promoted products "which, despite all of its efforts, failed to obtain consumer acceptance and . . . were withdrawn from the market."

Doan and McKeen Honored

Leland I. Doan, president of The Dow Chemical Company, and John E. McKeen, president of **Chas. Pfizer** & Co., were two of The Fifty Foremost Business Leaders of America honored November 6 by Forbes Magazine at the Waldorf-Astoria Hotel, New York.

The Tuberculosis Problem

We are somewhat confused by the statement of Dr. H. van Zile Hyde, chief of the Division of International Health, U.S. Public Health Service, before the 4th Pan-American Congress of Pharmacy and Chemistry November 8, that malaria, cholera, smallpox, diphtheria, typhoid fever and *tuberculosis* have been "all but eliminated" in the United States and other economically developed countries.

The reason for our confusion is that on November 1, the Washington office of the American Medical Association said:

"Although active tuberculosis has declined 30 per cent in the last five years, the general control picture is not entirely reassuring. This is the report of Public Health Service and the National Tuberculosis Association on results of the only nationwide survey in five years. The check shows that despite intensive efforts for control, almost 40 per cent of the active cases are unknown to health authorities, and these people are not receiving treatment. (Unknown cases are estimated on the basis of X-ray survey findings.) Other findings—In the five years there has been no decrease in the number of persons who are or have been ill with the disease, and there are still about 250,000 persons known to have tuberculosis in its active form. The most encouraging phase of the report is that active cases have dropped from 350,000 to 250,000 and inactive cases requiring supervision of health departments from 600,000 to 550,000."

In New York City it is reported that new cases pop up at the rate of more than 500 a month, but deaths are down 10 per cent from 1955. New York City was said to have 12,732 active cases at the end of last year, with another 4,000 undetected cases going around untreated.

Consumer Spending Increases

The percent of increase in consumer spending for 1956 was 38 over 1950. The increases in categories in which this industry is particularly interested are: Personal care expenditures (barber and beauty shops) 76.2 per cent; Medical care, overall 40.6 per cent; Payments to physicians 37.5 per cent; Hospital and sanitarium payments 76.5 per cent; Accident and health insurance 119.6 per cent; Burial expenses 91.8 per cent.

DCAT Dinner and Meeting

March 6, 1958 is the date of the 32nd Annual Dinner of the Drug, Chemical and Allied Trades Section of the New York Board. As usual the dinner will be held at the Waldorf-Astoria Hotel.

The Fall Annual Meeting of DCAT, which has been moving to different places in the Pennsylvania Pocono Mountains in an effort to find a place both suitable for the meeting and with sufficient capacity to accommodate all who wish to attend, is being moved to upstate New York next year. The place is the Sagamore Hotel, Bolton Landing, Lake George, N. Y., and dates are September 11 to 14, 1958.

Socialized Medicine Troubles

The British Socialized medical system causes doctors many troubles. Because a woman doctor got into a "muddle" over prescriptions, she had to return £72 to the Hertfordshire Executive Council. The doctor issued prescriptions for items covered by the drug capitation fee paid to her and issued other prescriptions she should have dispensed herself. She told the Council:

"I have been unhappy for some time about the muddled kind of way it seemed necessary to carry out my dispensing in the effort to give my patients their necessary medicines, but I was unaware I had committed any errors. It is extremely unsatisfactory and confusing, working in three counties, both prescribing and dispensing, keeping all accurately separate, and invoicing all legitimate expensive drugs always on a green form for the appropriate county."

In another instance, a Ministry of Health Appeal Board upheld an appeal by a doctor against Middlesex Executive Council which said that gin was not a drug it was bound to provide. The doctor prescribed the gin to make up a mixture of morphine and cocaine for a patient suffering from inoperable cancer. The Board said it was satisfied that gin produced a state of well-being which would not be given by retified spirit. "We think it is the function of a doctor to have regard to the mental state of his patient in a case like this," the Board stated.

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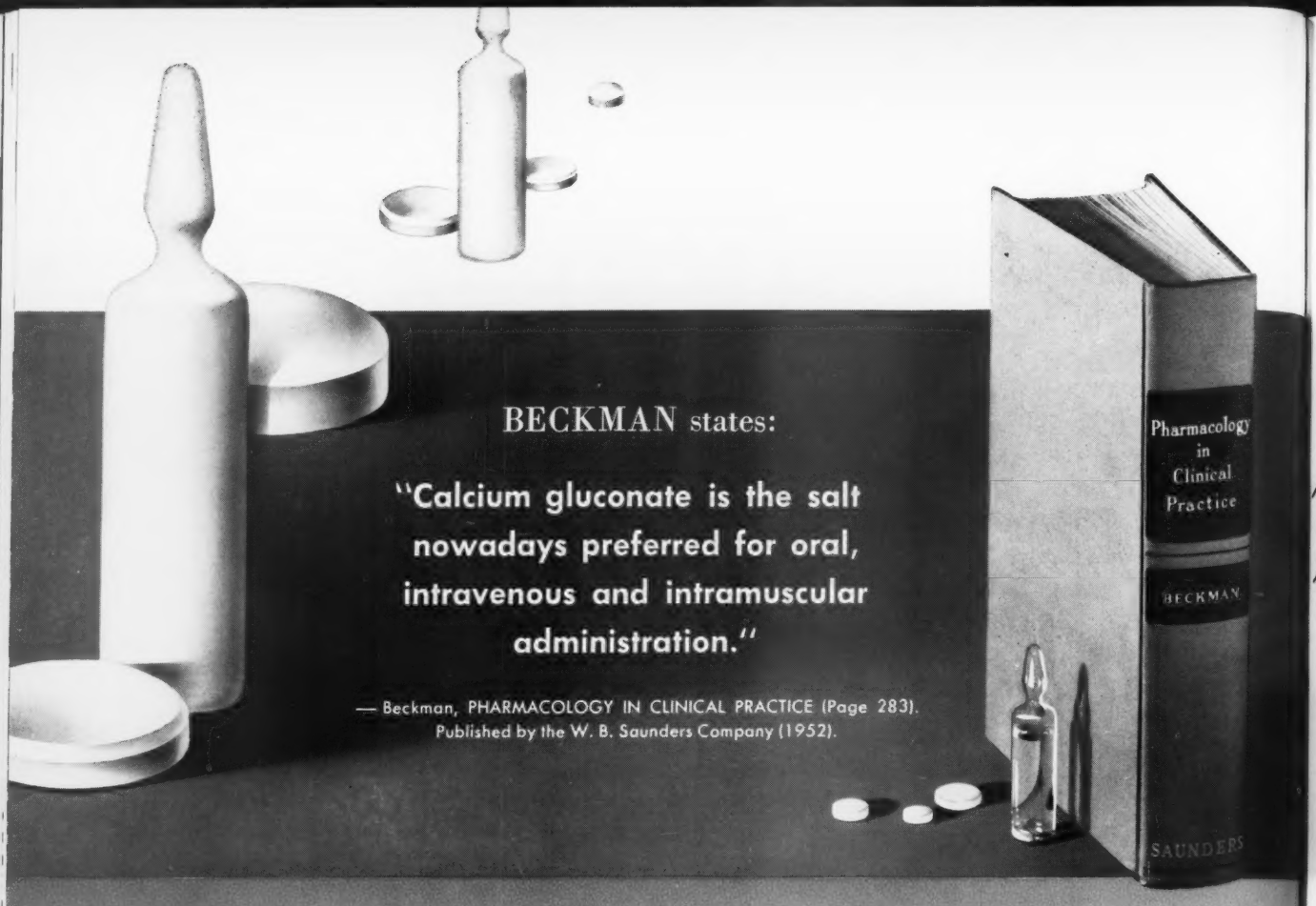
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— Beckman, PHARMACOLOGY IN CLINICAL PRACTICE (Page 283). Published by the W. B. Saunders Company (1952).
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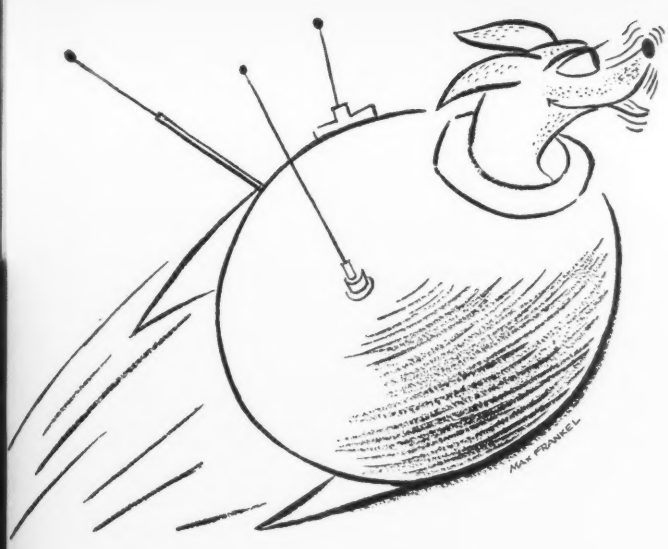


Member of the American Rocket Society, the British Interplanetary Society, and the Association of Lunar and Planetary Observers, Mr. Blish is a technical writer for Chas. Pfizer & Co., Inc. He is also the author of "The Frozen Year," a novel set against an International Geophysical Year background and dealing with satellite shoots.

SPUTNIK and Pharmaceutical Research

By JAMES BLISH

As man stands on the threshold of interplanetary space, he is confronted with four major medical problems whose scope is unknown, and for which there are few answers at present. The use of a live dog as part of the payload of Sputnik II is an obvious attempt on the part of the Soviet astronauts to find out more about these problems.

Briefly, the problems may be grouped under four heads: acceleration, radiation, orientation and decompression.

Of these, acceleration is the most familiar problem. High accelerations are readily attainable on the Earth, both in jet and rocket powered aircraft, and aboard such rocket-powered sleds as Col. John Paul Stapp rode until last year. Giant centrifuges, such as the model operated at John Hopkins in Baltimore, also have provided a great deal of data on how the human body behaves under accelerations as high as nine gravities.

In this field some answers have been coming through. It seems clear that very high accelerations, such as those required to reach cis-lunar or interplanetary speeds, can be born by the human body for brief periods—*but* as long as existing power plants require the use of such high accelerations, space travel is likely to remain a young man's game. No middle-aged man with partially hardened arteries or an undetected heart flaw is likely to live through such a flight. Later, when more power will make gentler takeoffs available, space travel may become possible for the middle-aged (say, a man over 25; acceleration in these ranges ages a man rapidly.)

The radiation problem is much more serious, and much less well understood. In addition to the extremely hard radiation to which a space travelling vehicle is exposed from the Sun, such a vehicle is constantly bombarded with primary cosmic rays—atomic particles of relatively large size and carrying an almost inconceivable energy load. There is at present no way known to shield the passenger of a space vessel from the more energetic of these fast particles. They are particularly damaging to the eyes—indeed, the probability is that a crew member taking a hit from a heavy primary in the eye or along the optic nerve would actually be able to feel the impact. Dr. Heinz Haber of the University of California, one of the few tentative experts in this difficult field, has predicted:

"The probability is that, if you have a manned space station with 50 people on it, you would wind up with serious damage, possibly in the form of a cataract, in one eye of one crew member inside of about a week."

And Dr. Schaeffer of the Navy School of Aviation Medicine has estimated that human tolerance of cosmic radiation cannot be greater than 15 hours a day. Thus the chances of making even a five-day trip to the Moon without serious cosmic-ray depredations do not look good at present.

The third problem, orientation, depends primarily on how the human organism will respond to being weightless—a question close to impossible to study on Earth, but one which will be the rule during most of any sort of manned space flight. All but a few moments of any space trip are made in free fall, a condi-

(*Continued on page 804*)

YLANG-YLANG
"The Flower of Flowers"

By STEFFEN ARCTANDER, PERFUMERY RESEARCH & DEVELOPMENT DEPARTMENT, COLGATE-PALMOLIVE CO., JERSEY CITY, N. J.

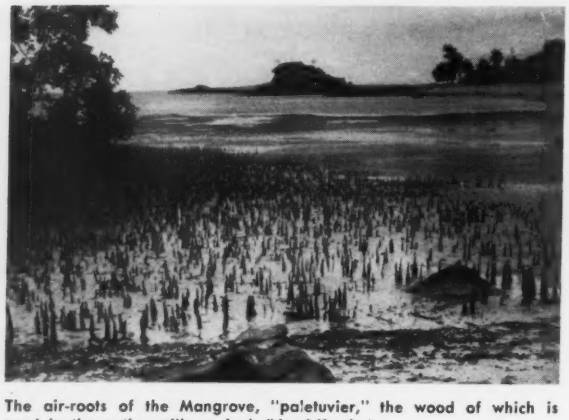
Among the explanations of the origin of the term ylang-ylang, the one most often used is, that this word in Malayan means "Flower of Flowers." It is so much more descriptive and romantic than all the other explanations. So let us presume—for a while—that this is the correct explanation.

Ylang-ylang trees have been known by European explorers for several hundred years, and in their habitat probably for a thousand years or more. During the century of great sea explorations in the far East, spices and perfume plants were among the booty aboard the returning French and other European ships. Spices as well as perfume plants were later shipped to those tropical islands, already occupied by the French, British, Dutch, Portuguese or Spanish immigrants. During the 1770's, a large number of spice seeds, seedlings, perfume plants and cuttings arrived in Reunion and Mauritius in the Indian Ocean, at that time French possessions. Among the plants were ylang-ylang cuttings from Ceram and other (now Indonesian) islands. The French explorers probably were aware of the fact, that the ylang-ylang tree will only produce odorous flowers, when the tree is cultivated, but not as wild growing. The settlers in Reunion were eager to exploit and cultivate the new land, and the Governor, Pierre Poivre (which means PEPPER!), himself being a botanist, engineer and explorer, encouraged this new agricultural progress and introduced several spices from his own Far-Eastern travels.

Probably because of insufficient know-how and economical means after the downtrend of power in the

A close-up of an Ylang-Ylang flower, which I hold in my left hand.

The foreman of this distillery displays one flower of Ylang-Ylang.



The air-roots of the Mangrove, "paletuvier," the wood of which is used in the native stills as fuel. (Nossi-Komba).

View from the SPPM-distillery in Nossi-Be. A line of copper stills is ready for the morning's crop of flowers.

A view of the Monier-plantation, Reunion. Note the crippled shape of the Ylang-Ylang trees. Palm trees act as wind breakers and sunscreen.

French mother country, the plantations were not increased nor fully exploited, and a definite lack of interest during the following century resulted in almost no production at all from Reunion island. Mauritius had abandoned all production of perfumes and spices, since the island became a British possession after Napoleon's defeat.

But towards the end of the 19th century, during the more fortunate decades for the French colonial regime, the ylang-ylang plantations in Reunion island were rapidly increased. At the culmination just before World War I, there were probably one-quarter million ylang-ylang trees in the island. Meanwhile, some prospective settlers had brought the tree to Madagascar, and to the small island of Nossi-Be, Northwest of Madagascar. Later on, the tree was introduced in the still more favorable climatic conditions, ruling in the Comoro Archipelago, midway between Northwestern Madagascar and the African East Coast. While production of ylang-ylang oil and ylang-ylang concrete in Reunion rapidly decreased since 1920, the plantations in Nossi-Be flourished until recently, when even this island was outproduced by the Comoro islands. Installations, which had been brought to Reunion shortly after 1900, was first brought to Madagascar and Nossi-Be, but the Comoro islands enjoyed a more direct sponsoring from France, when a very large French perfume house brought modern distillation and extraction equipment to these islands.

At least 90 per cent of all ylang-ylang oil produced in the world to-day, derives from the Comoroislands in the world today, derives from the Comoro islands and Nossi-Be. It is interesting to observe, how the center of production has moved westwards during the past 50 years. At the beginning of this century, the Manila brand ylang-ylang oil was considered superior to all other ylang-ylang oils, and there was a substantial production in the Philippines. Then the plantations in Reunion island started to assert themselves and soon outproduced the Philippines, but the Manila brand seemed to be almost immortal. Even in our day, more Manila ylang-ylang oil seems to be sold than is actually produced, until one day all the clients will realize, that the Philippine production is, at the most, only a couple of tons annually. When the tree reached Madagascar, where particularly the Northeast coast and the island of Nossi-Be were cultivated with ylang-ylang trees, the importance of Reunion as a producer decreased rapidly. Now we can see Nossi-Be's production being surpassed through the modern equipment production in the Comoro Archipelago.

Although I also met recent cultures of ylang-ylang

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The Comoro-freighter anchors up in Hellville, Nossi-Be, to take in some tons of Ylang-Ylang oil

Ylang-Ylang flowers arrive at the distillery at Monier-Saint-Pierre, Reunion. Above: Close-up of workers.

DR. ROBERT A. HARDT

Pan-American Pharmacy

The 4th Pan-American Congress of Pharmacy and Biochemistry met in Washington, D.C. early last month. Dr. Robert A. Hardt, of Hoffmann-La Roche, who served as chairman of the Organizing Committee, was elected president of the Congress. Other officers were: Newell Stewart, National Pharmaceutical Council, vice-president; George B. Griffenhagen, Division of Medical Sciences and Public Health, Smithsonian Institute, secretary-general; and S. Barksdale Penick Jr., S. B. Penick & Company, treasurer. Dr. Hardt presided over the Congress with a gavel made of 22 species of wood from each of the 22 nations belonging to the organization.

The Congress meets every three years in one of the 22 different countries. The next meeting will be the 5th Congress in Chile in 1960. The United States will not be host again for 66 years, or in 2023 A.D.

Numerous resolutions were proposed and many were passed. Some that were adopted recommended that drug specialties bear names related to active principles; that official preparations not be exploited as pharmaceutical specialties; that the ownership of a pharmacy be exclusively the right of a pharmacist; that pharmacies be the sole distributors of medicines; that drug labels bear dosage statements in readily distinguishable form; and that certain drug labels bear expiration dates. Several objectionable resolutions were passed by sections of the Congress, which after strenuous efforts on the parts of less prejudiced delegations, were tabled at the Plenary Session where all resolutions were required to be approved. Among these were resolutions which: Called for abolition of patents on drugs; would require drugs to carry retail prices on labels; and would eliminate exclusive distribution rights of drugs.

Another resolution which was adopted stated that the action taken by the Pan-American Medical Confederation at Bogota in 1955 is prejudicial to the professional obligations and responsibilities of the pharmacists and the pharmaceutical industry. The 1955 resolution referred to called for a study of the drug registration legislation of the various Latin American countries, the drafting of a model uniform code, and urged each nation to enact legislation which would simplify and expedite the distribution of drugs. This position met with the general approval of the U.S. industry. It is believed by some that the Pan-American Congress, which is composed largely of pharmacists, passed this resolution partly because of antagonism of some Latin American pharmacists toward doctors, and partly because of misunderstandings with regard to the Medical Confederation resolution, copies of which were not available to those working on the wording of the resolution. So the result is that a stand taken by physicians intended to make drugs more readily available throughout Latin America for treatment of the sick, is now opposed by an organization of pharmacists.

In the opening address, Dr. Hardt told the Congress: "We wish to share our knowledge with our colleagues and make people-to-people friendships in order to strengthen international understanding. Certainly a common interest in the health of the people of the world is a vehicle by which our communications can be improved." He also told them: "Great new discoveries are inevitable in the light of the intensive research now being carried on in the laboratories of the world."

Dr. Aims C. McGuinness, special assistant to the Secretary for Health and Medical Affairs, told the Congress: "In the United States the funds spent by the pharmaceutical industry on research have multiplied 10 times—I repeat, 10 times—in the short space of 20 years. Truly pharmacology has come of age. These developments make ever more necessary the meeting together in international congress of pharmacologists, related scientists, and representatives of in-

(*Continued on page 831*)

Proprietary Medicines in New York

The Joint Legislative Committee on Imitation Food Products and Problems of the New York State Legislature, known as the "Drumm Committee," because it is chaired by Assemblyman Willard C. Drumm, of Nieverville, N.Y., issued last month a report on "The Sale of Proprietary Medicines" dated March 30, 1957.

The report states that legislative enactments of the State "suffer from failure to define the terms 'proprietary medicines' and 'poisonous, deleterious and/or habit forming'. What the Legislature failed or neglected to enunciate, the Board of Pharmacy of the State of New York assumed to regulate by promulgating Rule 17, which, while it did not define 'proprietary medicines', did attempt to set up a standard for determining the term 'deleterious' as prepared medicine in the original package, the consumption of the entire contents of which would cause illness, would be considered harmful, deleterious or poisonous. It restricted the sale of such prepared medicines to only drug stores with a registered pharmacist in attendance. Such a definition in the opinion of the Committee was unrealistic. By this standard, almost every prepared and packaged medicine could be banned from any sales outlet outside of drug stores, providing the package or preparation was large enough . . . .

"It is the considered opinion of the Committee that these products known as proprietary medicines, are fully packaged medicines, labeled in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act which do not require a prescription for their purchase. We have all used many of these products on countless occasions since our childhood, and we know of their efficacy and harmlessness from personal experience. These harmless home remedies are sold without restriction in 40 states today. Some home remedies may be sold in other states or all may be sold in some areas of these states. Even in New York State, they may be sold with Pharmacy Board approval in rural areas if three miles distant from a drug store. The great majority of the people of this Nation have purchased these products from non-drug outlets with no ill effects on the public health. New York's registered stores have stocked and sold aspirin and milk of magnesia along with other drugs and medications with no ill effect on the health of our people. It therefore concomitantly follows, that if such sale in rural registered stores is lawful and for the public interest and health, an extension of authorization to sell such drugs and products in urban outlets would not create any different result.

"Plain common sense and reasoning shows conclusively that there is no casual relationship between ingestion of excessive amounts or the improper use of proprietary medicines to the manner in which they are purchased or place where the purchase is made. The fact is that all control over the usage and dosage of a proprietary medicine ceases with the completion of the purchase and delivery of the medicine across the counter. It matters not whether the proprietary drug or medicine is purchased in a drug store, a registered store or in a corner grocery; the fact is that when the purchaser walks out of the store, all control over the drug or medicine passes from the seller and from that time on the responsibility for proper usage rests entirely with the purchaser."

The report cites the New Jersey court decision of March 18, 1957 which held that the following fourteen products are non-poisonous: Vicks Va-Tro-Nol, St. Joseph's Aspirin for Children, Phillips' Milk of Magnesia Tablets, Anacin, Aspergum, Carter's Little Liver Pills, Bromo Seltzer, Bromo Quinine, Alka-Seltzer, Castoria, Ex-Lax, Sal Hepatica, Pepto-Bismol, Bufferin.

Also cited is the Minnesota decision of February 8, 1957, which the report says "is of like tenor and includes most of the products held non-poisonous by the New Jersey court. In that case the court said: 'That there is no evidence that the sale by the Red Owl Stores, Inc., or by anyone else, of any of the items concerned, is endangering, or may in the future endanger, the public health of the people of the State of Minnesota; and that there is no evidence that any of the items concerned has been, is, or may be, harmful to any individual.'

"The claim therefore, that unrestricted sale of these and other proprietary medicines in non-drug outlets would be harmful to the public health is without justification. The safeguards to be found in the Federal Food, Drug, and Cosmetic Act and the provisions of

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PASTEUR Fermentation Centennial

The importance of basic research to medicine and to the pharmaceutical industry was emphasized to both the public and the scientific community by the Pasteur Fermentation Centennial, held at the Waldorf-Astoria Hotel November 21.

The one-day scientific meeting, sponsored by Chas. Pfizer & Co., Inc. brought together 18 scientists from six countries—England, France, Cuba, Japan, and the USSR, as well as from various points in our own country.

The event that was celebrated is Pasteur's discovery that the fermentation of lactic acid is caused by living micro-organisms.

Proper understanding of the fermentation process also made it possible to put fermentation on a scientific basis, and to turn it from an art into a great industry. Today molds and bacteria are at work in fermentation tanks, producing important industrial chemicals, as well as such luxuries as beer, wine and sauerkraut. But more important, fermentation now figures in the production of all the antibiotics but one.

The more than 800 scientists—including two Nobel Prize winners—attending the Waldorf meeting heard, from their eminent colleagues on the program, some of the most recent applications, trends and new theories to develop out of Pasteur's finding.

The chairman of the conference was Dr. James A. Shannon, Director of the National Institutes of Health.

How Pasteur discovered the cause of fermentation was described by Prof. L. Pasteur Vallery-Radot, grandson of the great French scientist and president of the Pasteur Institute of France. Pointing out that this discovery led directly to Pasteur's monumental germ theory of disease, upon which much of modern medicine is based, Prof. Vallery-Radot concluded:

"Let us assess what this paper of Pasteur's contributed to biological science; he not only demonstrated that fermentations are a work of life, and not a work of death as had been maintained before him, but he also formulated what used to be called the *germ theory*, applicable alike to infectious diseases and to fermentations.

"He affirmed specificity. Had he not introduced the idea of specificity into the study of fermentation, his achievement would have been limited to discovering the role of microorganisms in fermentation generally.

This was the idea that enabled him to bring order into the study of the various fermentative processes, as it later enabled him to do so in the study of contagious diseases, and to dispel all the confusion and uncertainty of the past. And furthermore, did it not gratify his scientific mind, accustomed to assign to each effect a cause proper to it?"

The paper in which Pasteur announced this discovery is amazingly rich in scientific ideas which are only now beginning to be realized in modern science, Dr. Rene J. Dubos of the Rockefeller Institute for Medical Research pointed out.

"Pasteur was only 34 years of age when he wrote the *Memoire sur la fermentation appelee lactique*, which appeared in December, 1857. This publication, his first on biological problems, can truly be regarded as the manifesto of the Germ Theory, heralding the century of spectacular achievements that we are celebrating today . . .

"It is true that the 1857 Memoire does not provide any proof of the germ theory of fermentation. At the most it points to some vague analogies between the growth of yeast during alcoholic fermentation and the phenomena accompanying the appearance of lactic acid in fermenting natural products. But it is a historical document nevertheless because it states in a forthright manner, albeit in the form of unproven assertions, the fundamental concepts from which evolved the theory and methodology of microbiological sciences . . .

"The Memoire provides also an unequivocal statement of the influence that acidity, neutrality, and alkalinity exert on the growth of the various ferments and on the course of fermentation . . . There is also a hint, as it were an omen, of the selective effect of antiseptics . . .

"The idea of a specific ferment associated with each fermentation, of disproportion between the weight of the ferment produced and the weight of matter transformed, of vital competition between two organisms which simultaneously invade the same medium, resulting in the dominance of the one best adapted to the culture conditions—all these ideas, which the future was to prove valid and develop into a body of science and technology, are forcefully set forth in this short and almost amateurish paper . . .

"Pasteur retained throughout life the ability to see beyond evidence and to dream of romantic scientific concepts even when they appeared at the time to go counter common sense. But he was also a masterful experimenter and he possessed to an extreme degree the power to observe the unexpected and to let concrete facts bring his activity back to the level of the possible . . .

"The discovery of stereoisomerism; the studies on spontaneous generation; the recognition of anaerobiosis and of the metabolic phenomenon now called the Pasteur effect; the improvements in practical techniques for controlling acetic and alcoholic fermentation in the manufacture of vinegar, of wine and of beer; the development of pasteurization for preserving beverages and foodstuffs; the control of silkworm diseases by hygienic procedures; the spectacular feat of producing immunity against bacterial and viral infections by attenuated vaccines; all these constitute a range of theoretical and practical achievements as broad and epoch making, both in originality and implications, as has ever come out of a single human brain . . .

"Pasteur never refrained from boldly stating his views and hypotheses—even when he knew that he lacked supporting evidence—witness the 1857 Memoire on lactic acid fermentation. In most of his formal papers, as well as in the course of many casual remarks, he was wont to outline projects of research which were close to his heart, but which circumstances did not permit him to undertake or compelled him to

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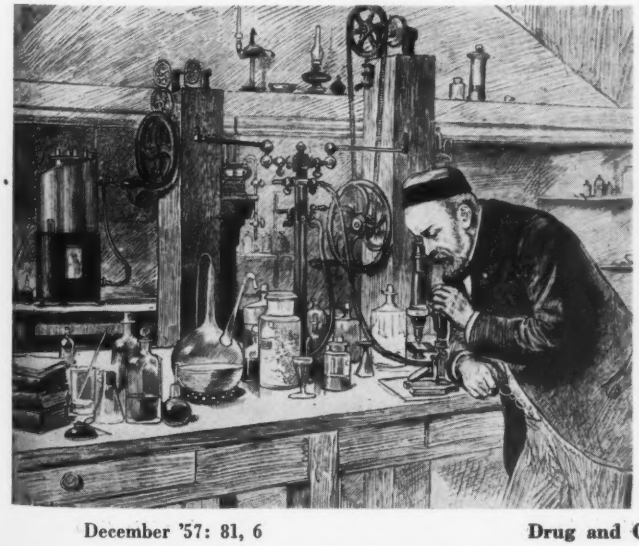


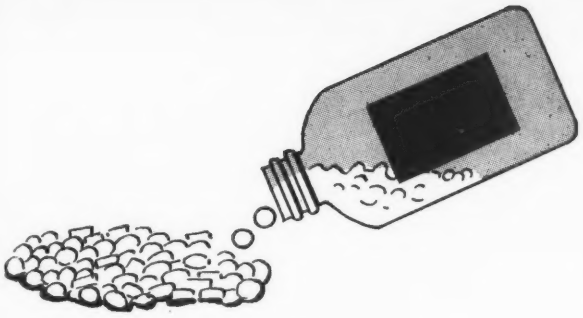
The United States Tariff Commission has published the figures on the production, sales, and values of synthetic organic chemicals for 1956. The following are the ones in which this industry is primarily interested.

Synthetic Drugs and Chemicals 1956

Acetylsalicylic acid production in this country in 1956 totaled 16,603,000 pounds, compared with 15,092,000 pounds in 1955. Sales for 1956 totaled 13,524,000 pounds, valued at $7,007,000, with a unit value of 52 cents, compared with 1955 sales of 13,203,000 pounds, valued at $6,955,000 with a unit value of 53 cents. Production of salicylic acid in 1956 totaled 7,589,000, against 1955 production of 7,768,000. However, 1956 sales were higher at 6,585,000, valued at $2,373,000, against 1955 sales of 5,227,000, valued at $1,923,000. Salts of salicylic acid were almost 50 per cent lower in 1956 to the amount of 969,000 pounds, against 1,880,000 in 1955. Production of sodium salicylate fell off sharply in 1956 to 776,000 pounds, from 1,838,000 pounds in 1955.

Sulfa drug production was up in 1956 to 3,817,000 pounds, compared with 2,767,000 pounds in 1955. Antihistamines of the cyclic type were produced in 1956 to the amount of 211,000 pounds, against 151,000 pounds in 1955. Sales in 1956 totaled 86,000 pounds, valued at $2,309,000, compared with 61,000 pounds, valued at $1,748,000 in 1955. Production of antihistamines of the benzenoid type in 1956 totaled 74,000 pounds—there is no 1955 figure given. Production of barbituric acid and derivatives for 1956 was lower at 756,000 pounds, compared with 864,000 pounds in 1955. However, 1956 sales were lower at 467,000 pounds, valued at $2,483,000, against 1955 figures of 486,000 pounds, valued at $2,807,000. Phenobarbital production of 292,000 pounds, and sales of 240,000 pounds, valued at $794,000, were all lower than 1955 production of 431,000 pounds, and sales of 292,000 pounds, valued at $1,017,000.

Vitamin production and consumption was higher for all except thiamine and pantothenic acid, the first of which was lower in sales, and the second of which was lower in production. The figures for vitamins are: Vitamin A, production for 1956 196,621 billion units, against 170,429 billion units for 1955, sales 1956 166,221 billion units, valued at $15,278,000, against 162,348 billion units, valued at $15,344,000 for 1955. Vitamine B_1 production 1956, 266,000 pounds, against 234,000 pounds for 1955; sales 1956, 168,000 pounds, valued at $4,228,000, against 180,000 pounds, valued at $7,048,000 for 1955. Vitamin B_2 for human consumption, 1956 production 164,000 pounds, against 136,000 for 1955; sales 1956, 101,000, valued at $2,493,000, against 95,000 pounds, valued at $3,349,000 for 1955. Vitamin B_2 for animal and human consumption, production for 1956, 206,000 pounds, against 175,000 pounds for 1955, sales for 1956, 144,000, valued at $2,828,000, against 123,000 pounds, valued at $3,065,000 for 1955. Vitamin B_6 production 1956, 37,000 pounds, against 30,000 pounds in 1955; sales for 1926, 24,000 pounds, valued at $3,615,000, against 1955 sales of 23,000 pounds, valued at $4,448,000. Vitamin B_{12} production for 1956, 655 pounds, against 488 pounds for 1955; sales for 1956 totaled 450 pounds, valued at $22,640,000, against 357 pounds, valued at $20,614,000 in 1955. Ascorbic acid and derivatives



production for 1956, 2,866,000 pounds, against 2,354,000 pounds for 1955; sales for 1956, 2,445,000 pounds, valued at $12,884,000, against 2,154,000, valued at $15,005,000 for 1955. Pantothenic acid and derivatives production for 1956, 517,000 pounds, against 555,000 pounds for 1955; sales for 1956, 294,000, valued at $2,485,000, against 264,000 pounds, valued at $3,225,000 for 1955. Vitamin K production for 1956, 8,000 pounds, against 4,000 pounds for 1955; sales for 1956, 4,000, valued at $52,000, against 2,000 pounds, valued at $29,000 for 1955.

Steroid hormones production for 1956, 56,000 pounds, against 41,000 pounds for 1955; sales for 1956 totaled 26,000 pounds, valued at $25,908,000, against 12,000 pounds, valued at $27,865,000 for 1955. In 1956 there was produced 7,000 pounds of hydrocortisone, and 4,000 pounds of prednisolone. Sales of hydrocortisone in 1956 totaled 4,000 pounds, valued at $9,552,000, and sales of prednisolone in 1956 totaled 1,000 pounds, valued at $7,455,000.

Caffeine production was higher for 1956 at 1,758,000 pounds, against 1,153,000 pounds for 1955. Sales were higher for 1956 at 1,640,000 pounds, valued at $4,783,000, compared with 1,238,000, valued at $3,673,000 for 1955.

Salicylamide production for 1956 was up to 374,000 pounds, from 274,000 pounds for 1955; sales were 370,000 pounds, valued at $451,000 for 1956, 1955 figures not given.

Antibiotics for human and veterinary use production for 1956 totaled 1,967,000 pounds, against 1,572,000 pounds for 1955; sales for 1956 totaled 1,737,000, valued at $271,371,000, compared with 1955 figures of 1,367,000 pounds, valued at $242,392,000. Note: Sales of antibiotics include all forms—diluted or undiluted—in bulk or in packages.

Penicillin salts production for 1956 totaled 631,000 pounds, against 455,000 pounds for 1955; sales for 1956 totaled 593,000 pounds, valued at $63,529,000 against 445,000 pounds, valued at $43,980,000 for 1955. Streptomycin production for 1956 totaled 130,000 pounds, against 154,000 pounds for 1955; sales for 1956 totaled 147,000 pounds, valued at $5,604,000, compared with 99,000 pounds, valued at $5,127,000 for 1955. Dihydrostreptomycin production for 1956 totaled 492,000 pounds for 1956, compared with 369,000 pounds for 1955; sales for 1956 totaled 431,000 pounds, valued at $18,198,000, against 332,000 pounds, valued at $16,318,000 in 1955.

Tetracycline production in 1956 totaled 220,000 pounds; sales totaled 186,000 pounds, valued at $72,903,000. No figures are given for 1955. Neomycin base production for 1956 totaled 17,000 pounds, against 15,000 pounds in 1955; sales for 1956 totaled 14,000 pounds, valued at $5,989,000, against 11,000 pounds, valued at $5,222,000 for 1955.

Among the flavoring and perfume materials, methyl salicylate production for 1956 totaled 3,518,000 salicylate production for 1956 totaled 3,518,000 pounds, against 3,130,000 pounds in 1955; sales in 1956 totaled 3,283,000 pounds, valued at $1,664,000, compared with 1955 figures of 3,398,000 pounds, valued at $1,623,000. Synthetic menthol production for 1956 totaled 382,000 pounds, against 261,000 pounds in 1955; sales in 1956 totaled 292,000 pounds, valued at $1,579,000, compared with 274,000 pounds, valued at $1,642,000 in 1955.

Coumarin production in 1956 totaled 780,000 pounds, and sales totaled 660,000 pounds, valued at $2,000,000. No 1955 figures are available. Safrol production for 1956 totaled 194,000 pounds, against 315,000 in 1955; sales for 1956 totaled 39,000 pounds, valued at $39,000, compared with 120,000 pounds, valued at $154,000 for 1955.

Ionones production for 1956 totaled 271,000 pounds, against 266,000 pounds for 1955; sales for 1956 totaled 238,000, valued at $927,000, compared with 198,000 pounds, valued at $716,000 in 1955. Methylionones production in 1956 totaled 249,000 pounds, against 205,000 pounds in 1955; sales in 1956 totaled 226,000 pounds, valued at $1,283,000; compared with 180,000 pounds, valued at $960,000 in 1955.

Geraniol production in 1956 totaled 381,000 pounds, compared with 462,000 pounds in 1955; sales in 1956 totaled 279,000 pounds, valued at $951,000, against 427,000 pounds, valued at $1,186,000 in 1955. Hydroxycitronellal production in 1956 totaled 200,000 pounds, against 116,000 pounds in 1955; sales for 1956 totaled 154,000 pounds, valued at $923,000, against 123,000 pounds, valued at $702,000 in 1955. Linalool production in 1956 totaled 58,000 pounds, against 85,000 pounds in 1955; sales in 1956 totaled 54,000 pounds at $270,000 in 1955. Linalyl acetate production in 1956 totaled 110,000 pounds, against 115,-

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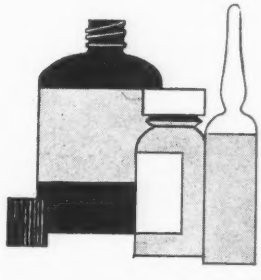

Pharmaceutical Flavoring*

BY MARVIN K. COOK CONSULTING CHEMIST

Palatability of an oral medicament is an essential in progressive pharmaceutical manufacture. With a potent drug, an antacid or a vitamin preparation, acceptance by the consumer is influenced by aroma and flavor. To assure consistently high acceptance, considerable effort must be expended to standardize and control odor and taste.

The careful selection of appealing flavors for medicinal preparations is certainly worth the effort. Panel testing methods, developed originally by the food industry as a parameter of consumer acceptance, have also proved helpful in pharmaceutical compounding, particularly with mass market products.

Some pharmaceutical laboratories remain unconvinced as regards panel testing methods and the validity of the findings. In this case, selection of a flavor often becomes the responsibility of the pharmaceutical chemist or members of the executive staff who may personally lack the necessary sensory perception and training to pass critical judgments on flavor differences. Recent studies have shown that the ability to "taste" and the width of the taste spectrum vary markedly in different individuals and are most often predetermined genetically. It is probable that "taste blindness" in various degrees occurs even more frequently than color blindness.

Taste panels serve a necessary function, in the absence of accurate and dependable objective techniques, to evaluate and standardize subjective responses. Panel testing also serves in quality control by providing a standardized method of evaluating raw materials and finished products. Select consumer panels comprising unprofessional groups are a further step in verifying professional panel judgment.

Flavor evaluation often requires the assistance of an expert. A flavor expert cannot accurately predict that the flavor will prove successful in a large consumer market. He can perform a very vital function in evaluating differences between flavors, in detecting adulteration, and can detect early deterioration and other off-qualities.

In contrast to food manufacturing where the constant attempt is to make good tasting products taste better, the problem in pharmaceutical manufacture is often to make unpleasant oral medicaments more palatable so that the patient will accept rather than endure the product.

Successful flavoring of pharmaceutical preparations hinges upon a number of factors. Of prime importance is the painstaking selection of a flavor that is truly harmonious with the product. Another point for consideration is the effectiveness of the flavor in masking undesirable tastes contributed by the medicinal. A third factor and perhaps the most difficult to apply is the utilization of the undesirable medicinal taste as a base upon which a palatable formulation is built. This is comparable in a way to perfume compounding in which traces of malodorous compounds such as indol and styrolyl acetate are employed to obtain an attractive character.

The physical attributes such as body (viscosity), texture and color in liquids, powders or tablets contribute markedly to flavor sensation, compatibility and retention. To illustrate, a wintergreen flavor that serves admirably in an elixir may seem weak and insipid in a tablet or overly strong in an emulsion. A remarkable improvement in a mint flavored antacid tablet containing a high percentage of calcium carbonate is accomplished by the addition of an amino acid.

Flavor strength will vary considerably in different solvents and the concentration to be used must be determined empirically. A freshly flavored product may undergo change in taste when aged, sometimes yielding an entirely different effect from the original. In general, the flavored mixture improves when it is allowed to stand for a week or longer. This is particularly true in the case of flavored tablets.

Many flat-tasting flavors may be brought to life simply by the addition of natural or artificial sugars. Here again, the quantity of flavor will vary depending upon the type and concentration of sugar used. For this reason, it is wise not to discard a flavor compound as unsuitable unless it is tested at different sweetness levels.

Further heightening of the flavor may be accomplished with traces of salt, citric acid, glutamic acid, monosodium glutamate, glycyrrhiza and various oleiomonosodium glutamate, glycyrrhiza and various oleoresins. Microscopic quantities of oleo-resins such as capsicum, ginger and vanilla will produce interesting effects in a flavored mixture and generally escape de-

*From a forthcoming book by Joseph Kalish and Marvin K. Cook.

COURTESY LEDERLE LABORATORIES

tection when subtly employed. Licorice extract may be prepared in tincture form, well aged, and used as an excellent material to shade flavor blends.

The use of vanilla and vanillins as a flavor base is deservedly popular. When these are properly employed, a mellow tonality is imparted to the finished mixture and these flavoring materials blend well with most essential oil mixtures. The fixative properties of vanilla and vanillins are well known and they may be used not only to stabilize flavors but also to repress certain undesirable tastes.

In flavor compounding, consideration must be given to the fact that there are different grades of the same essential oil. Peppermint, for example, can be obtained in types having a pungent menthol background or a sweet, mellow, almost molasses-like quality. Climatic variations, soil differences and distilling methods all contribute to variations in essential oils and their careful selection in formulation is of utmost importance.

Weeds in peppermint and spearmint crops will often contribute a disagreeable odor and taste to the distilled oil. As little as one per cent ragweed oil will produce a very unpleasant weedy or moldy taste in pharmaceutical products which may develop weeks after packaging. Fortunately, the disagreeable components of peppermint and spearmint oil are most often found in the first or lowest boiling fractions of the oil and can be removed by vacuum steam redistillation. In the case of peppermint oil, the first fraction will contain dimethyl sulfide, an unpleasant-smelling natural component, but a first fraction cut of 0.5 per cent will remove practically all the dimethyl sulfide and leave a much improved oil.

In the case of bad-tasting medicinals, the tendency has been to overflavor, particularly with strong aromatics. This is often a practice open to question and more efforts should be made, where possible, to blend with other materials such as the vanillins, glutamates, sugars and various flavor compounds.

Considerable efforts are expended by the pharmaceutical manufacturer in the creation, testing, production and sale of his products. Equally important but frequently neglected is the proper handling and storage of essential oils and other flavoring materials, even though they often represent the most sensitive and perishable constituents in the formula.

Progressive manufacturers make it a sound practice to buy the finest essential oils and flavor compounds available, since experience has shown that the off-qualities of an oil are frequently augmented in the finished product. This may be detected either immediately or during aging. Extended bulk storage of oils of questionable quality may also result in substantial financial loss because of deterioration. The purchase of inferior oils for pharmaceutical flavoring is false economy.

The general constituents of essential oils are the terpenes, oxygenated compounds, sesquiterpenes, and non-volatiles in the form of waxy or viscous residues. The odor and flavor effect is derived primarily from the oxygenated compounds. The terpenes for the most part do not contribute greatly to the odor value and are responsible for the difficulties experienced with essential oils. The terpenes are readily susceptible to oxidation in the presence of light and moisture and reduce the over-all solubility of the oil on aging. Ter-

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Pharmaceutical market research is still a young profession. In my opinion market research cannot be expected to make final recommendations and decisions. It acts, however, not only in an advisory capacity to management, but also as a balance to too great enthusiasm by medical research and sales departments. As such it carries a great deal of weight in the decision whether to market a product, and its influence can be felt for a long period of time. Rather a heavy burden is placed upon those concerned with it, not only as far as the welfare of the firm they serve is concerned, but also as it applies to the individual patient. A new product will no doubt be used on thousands of persons, and it is the welfare of the individual which we always have to keep in mind.

Medical Research for

BY PAUL DE HAEN

You may ask, what does promotion have to do with market research? It is not the direct function of your department to carry out promotional activities, but you are called upon to evaluate the sales possibilities of a new product in the early stages of its development. One of the most important phases of this evaluation, aside from ascertaining the total size of the market and the competitive situation, will be a review of the comparative therapeutic claims that can be made for your product. These therapeutic claims will decide whether your preparation is inferior, equal, or superior to other products available, and whether the physician can be persuaded to successfully prescribe it to his patients.

You may say that it is up to the medical department of your firm to develop therapeutic claims. This is no doubt true, and I am not advocating that you should attempt to tell your research people how to carry out medical research. That is their domain. But the market research group is the first contact the new product has with the harsh commercial world. If you are easily sold by enthusiastic statements and the sometimes wishful thinking of an investigator, you can ruin the entire career of a budding product, and this at great expense to its sponsor. Because of the records you keep you know more about the difficulties a new product is up against, and you are perfectly justified in pointing these out, and in demanding the best evidence you can obtain to advise your management accordingly.

Because very few market research people in the industry have had a medical or pharmaceutical professional background, you cannot be expected to evaluate research data for promotional purposes single-handed. You need the assistance of your research and medical departments of whom you can ask some very specific and pertinent questions, the answers to which you can use as your guide. These questions will vary with different groups of products, but there are some basic questions which apply to all products. There is one underlying thought which I believe you should always keep in mind in all your deliberations: What do these data mean to the practicing physician?—Will they aid him in successfully prescribing the product? If you keep this thought before you, the major part of your difficulties will disappear.

Let us now see what are some of these basic questions which you should ask yourself and to which you should seek the answers from your research people, so that you can advise your management whether the new product has a chance of being promoted successfully in a competitive market.

1. **Basic Pharmacology.** This concerns primarily toxicity studies and an investigation of the physiologic effect of the compound. Some of the work will have been carried out before you even know of the existence of the preparation. There are four aspects of pharmacology that are of interest to the sales department and to the practicing physicians.

First, have the studies been made in the various species of animals?

Second, have the results been compared with the action of other products?

Third, has the work of your laboratory been confirmed by other investigators?

*Presented to Eastern Pharmaceutical Market Research Group, New York, October 30, 1957.

Promotional Purposes*

Fourth, is the product of sufficiently low toxicity to be safe for human use?

I would like to add a word regarding the considerations of toxicity of a new drug. One frequently reads in the literature: This drug is non-toxic. Don't be fooled by it—it ain't so. There is no drug or food that does not produce some form of toxicity, depending upon the amount ingested. It is the relationship of the therapeutic to the toxic dose, or, in animals the medium lethal dose, that counts. With some drugs the dosage difference is greater, with others smaller, and the latter require more caution in administration.

2. **Clinical Evaluation.** This is sometimes also called human pharmacology. The results obtained will reveal the real value or lack of value of a new product. Here we find a number of basic questions which the physician user likes to see answered, and which are more or less alike for all products.

a) **Reputation of Investigators.** Who are the investigators who studied the product? Does their name carry weight with the profession, the specialist and the GP? Have they published previously in this field? Will their judgment be respected? A recent unfortunate example in this respect was the publication of a single report on a most important new indication of an old drug. The investigator was known by others to have made errors in previous investigations. The manufacturer, however, was carried away with the investigator's enthusiasm, and promoted the new use widely. Eventually the new claim had to be withdrawn, with loss of prestige for the manufacturer.

b) **Residence of Investigators.** Do the investigators all reside in one area, or are they distributed over the country? You will find that local conditions are an important consideration for product acceptance. An M.D. in California may be influenced more readily by the conclusions of a western investigator than by someone from New York.

c) **Publication of Report.** Is the report that has been submitted to your research department to be published? This may seem at first to be an odd question. But when you look at the advertising of recently introduced products, you may find quite often the statement in the bibliography: E. H. Smith, Personal Communication. The use of these "personal communications" is sometimes prompted by the fact that it takes so long to have a paper published in a medical journal, and the manufacturer wishes to make use of the data at an early date. On the other hand, many "personal communications" are never intended for publication.

In my opinion unpublished reports have a definite sales value if one can say in the bibliography "to be published" or "accepted for publication" or "in press." But beware of the "personal communication." Frequently it is merely the statement indicating the use of a product in a given number of patients which is primarily needed for inclusion in a New Drug Application.

Recently I had occasion to check with four physicians whose names appeared in the bibliography of a folder on a new product as authors of "personal communications." None of these investigators were going to publish their results, and only one indicated he would use the product in the future in selected cases.

(*Continued on page 845*)

Testing the Effect of Soaps and

BY O. JACOBI, Ph.D., KOLMAR RESEARCH CENTER, MILWAUKEE, WISCONSIN

The huge field of the cleaning agents and detergents can be roughly divided into three groups:

The first group is represented by the products which are used for the cleansing of the human skin.

The second group is represented by the materials which are used for technical cleaning purposes, such as laundering, dish washing and technical cleaning in industry and household.

A third group which, however, can also be looked at as a part of one of the two above mentioned, is the group of all surface active materials which can be used as emulsifiers.

The problem of the influence of the detergents on the skin would be much simpler if we only had to deal with the first group. Unfortunately, the technical cleaning agents and detergents come in contact with the human skin where they very often cause undesired side effects.

From the point of view of the skin, an ideal cleaning agent and detergent would be one which would clean thoroughly but not interfere with the normal physiological metabolism of the skin. The action of detergents on the living skin have been studied by different groups for years. Attempts have been made to answer this complex question with many different methods.

The following deals with a description of the principles of a number of methods which have been used and seem to be helpful in clearing up the problem.

Skin Cleansing

To judge the cleaning effect of soaps and detergents on the skin, R. and F. Jaeger[1] use the top light microscope employing the Leitz Ultrapak to check the skin surface before and after washing. This method gives only qualitative results. However, if micro-photographs are taken, they result in very impressive permanent records. L. Peukert and W. Schultze[2] use a reflection photometric method. As artificial soil they use a fluorescent mineral oil. The fluorescence of the oil is measured under a Woods Light with an electrical photometer before and after the cleaning. This gives quantitative numerical results.

A relatively simple method is based on the use of an oil soluble dye as artificial soil by painting a given area of skin with a weighed amount of such dye. The skin is then washed with the cleaning agent. After the washing the remaining dye is removed from the skin with a suitable solvent. The solvent solution is then colorimetrically evaluated according to the method described by B. Schmidt and R. Straub[3].

The methods mentioned so far leave the washing procedure up to the test persons. O. Jacobi[4] tries to eliminate the influence of the tester by mechanizing the washing procedure so that it is entirely independent of the individual tester. An open cylinder is fixed on the artificially soiled skin area. A measured amount of cleaner solution is placed in this cylinder. By bubbling a constant air current through the solution it is put in constant movement. This mechanical movement is similar to the one in a washing machine. By adding measured amounts of rinse water which circulates through a certain tube system, the rinsing is also mechanized. W. Blaich and U. Gerlach[5] have tried to improve this method by replacing the air current with a rotating stirrer.

All of these methods only yield relative values. The results depend on the surface conditions of the skin used (washability of the skin), as well as on the experimental problem of soiling.

Effect on Skin

Now going on to the methods of observation of the effects of detergents and soaps on the skin we first of all have to deal with the clinical picture of skin changes. Strictly subjective clinical observations of skin changes are always the first, but many times the only, possible test method. However, to be able to numerically record gradual differences, several authors as, for example, H. Koehler and R. Herrmann[6] have created certain scoring systems. One system judges the skin surface as: Good, smooth, rough, very rough and gives a number value to these different conditions.

Another help for the clinical observation is the close-up photograph of the skin surface. Naturally, a comparison should always be made with untreated skin.

To be able to catch details and also see small defects, the skin microscope is very helpful. The Leitz Ultrapak has proven to be a very good skin microscope. With this microscope the illumination of the skin area is vertical in the direction of the objective. The objective is enclosed in a ring condenser which focuses the light exactly at the skin underneath the objective. This vertical illumination has the advantage of excluding shadows which cannot be avoided if the illumination comes from the side. Side illuminated top light microscopes give distorted and false pictures by their shadow building. R. and F. Jaeger[7] have studied the influence of detergents on the living skin with this method. They have improved this method by staining the skin with fluorescent dyes.

Another method for the observation of the skin surface is the dermatogram developed by Bettmann[8]. According to W. Schoenfeld,[9] dermatograms are best made by applying an even film of printers ink on the

skin surface. A print of the skin surface is then made on a high gloss paper utilizing very little pressure. These prints can be evaluated directly as negatives or as positives after contact prints have been made. Schoenfeld always recommends that the dermatogram of the questionable skin area should be compared with one of unchanged neighboring skin. Specifically, he calls attention to the importance of the observation of the border line between treated and untreated skin areas.

Minute changes on the skin surface can be determined qualitatively as well as quantitatively by the "light cut" method developed by H. Koehler and R. Herrmann.[10] The procedure originally used in metallurgy for the testing of metal surfaces is based on the following facts:

A lighted slit is projected on the skin by a microobjective at an angle of 45° and observed with another microobjective and an ocular again at an angle of 45°. The optical axis of both systems, namely the slit projection and observation system, stand at an angle of 90° to each other. In this way a picture of the skin surface is received as if a histological cut has been made. If these pictures are photographed they can be used to determine the roughness = R as follows:

Detergents on Live Human Skin

$$R = \frac{k}{s}$$

In this formula, k is the length of the "light cut" curve, s is the length of a straight line from the beginning to the end of the curve. The bigger the value of R the rougher the skin. For an ideal smooth skin R would be 1. The difficulty of this method is to find exactly the same skin spot before and after the treatment.

Beside roughness or scaliness of the surface, the second macroscopically visible skin reaction from detergents is erythema. Measurements of erythemas, before and after the influence of detergents, have been done by J. Jambor.[11] He uses an electrophotometer with red and green filters. However, since the thickness the swelling of the horny layer as well as other factors influence the light reflection, the author could not get satisfactory results. His results were only reproducible on persons with very little or no hyperkeratosis.

Reflection measurements of the skin surface over the whole spectrum are described by Jacquez, Cuppenheim and co-workers.[12]

A different principle to measure the blood flow in the skin is used by Hertzman.[13] He employs the fact that the light absorption of tissue varies with the blood amount present in the tissue. He fixes a light source and a photoelectric cell, both light-tight but isolated from each other, side-by-side on the skin surface. The light source radiates light into the skin. The light diffuses through the tissue and is emitted again. The photocell registers the amount of emitted light. The amount of emitted light is related to the amount of blood present in the tissue. All these methods depend very much on each individual tested.

An answer to the question, how far detergents influence physiological conditions on the skin surface, will be given by the following methods.

Buffer Capacity of Skin and pH

As Wacek[14] has very impressively shown in a graph, the acid mantle is in the first line of the defense mechanism of the skin. Observations on the Influence of detergents on the pH of the skin are therefore of great importance. Originally the pH of the skin was determined with indicators. Later on the quinhydrone and calomel electrode were introduced by Schade and Marchionini.[15] The glass electrode was first used by Blank.[16] Today the glass electrode is exclusively employed since it has been possible to produce very thin but still relatively solid glass membranes. Also, the employment of electronic amplifiers in the pH meters make this method very popular. The Beckman special glass skin electrode and calomel electrode are both as thin as a pencil and allow the pH to be determined on very small skin areas. Skin pH measurements are a relatively simple way to investigate the acute influence of detergents on the normal acid mantle of the skin. By measuring the regeneration time of the acid mantle, intensity of this influence can be evaluated. However, there are two factors which have to be watched very closely in this type of testing. One is the fact that even an ordinary water rinse can change the normal skin pH since the water dissolves all or part of the compounds on the skin surface which are responsible for its pH. On the other side, the complete removal of detergent from the skin surface is essential to obtain correct pH values. The importance of skin pH changes caused by soaps and detergents has been over-rated many times. Therefore, changes in skin pH caused by detergents should only be negatively rated if the regeneration time is greatly prolonged and other skin tests have also been positive. This is especially true since, for example, on the other side the preservation of a normal pH by a slightly acid detergent does not give a guarantee that the detergent is harmless.

Also the alkali neutralization capacity discovered by W. Burckhardt[17] belongs in the defense mechanism of the skin surface. F. Laube,[18] O. Jacobi[19,20,21] and others, have repeatedly studied the influence of soaps and detergents on this skin function. The measure-

ment of the skin pH shows only the actual pH ion concentration on the skin surface. The alkali neutralization capacity determination, however, gives an idea about the potential conditions on the skin surface in regard to a forced change of its normal reaction. The principle of Burckhardt's method is the repeated neutralization of small amounts of sodium hydroxide on the same skin area using phenolphthalein as an indicator and measuring the time the skin needs to neturalize the alkali.

Koch[22] uses a different method for the same purpose. A glass cylinder open on both ends is fixed on the skin surface and filled with 1 c.c. of a 0.002 N sodium hydroxide solution. In intervals of five minutes during a period of thirty minutes the pH changes of the solution in contact with the skin are measured with a quinhydrone electrode.

Vermeer[23] uses 0.1 N sodium or potassium hydroxide solutions placed in rubber gloves covering the hands and forearms. Every five minutes he renews the solutions. This is repeated five times. Then he titrates an aliquot part of each of the solutions that was in contact with the skin using 0.1 N hydrochloric acid and phenolphthalein.

As can be expected of an amphoteric protein, the skin not only has an alkali neutralization capacity but it also has an acid neutralization capacity. The influence of modern cleaning agents and detergents which are able to work in an acid medium makes the study of this function of the skin very important. Schmidt[24] measures the acid neutralization capacity of the skin by determining the change of the pH of a 0.002 N sulfuric acid solution in contact with the skin employing a quinhydrone electrode. A similar procedure has been described by Epprecht[25]. He, however, uses a glass electrode. He measures the pH change of one drop of 0.015 N sulfuric acid solution which is in contact with the skin for one minute. He repeats these measurements ten times on the same skin area but always employs a new drop of acid.

Schuppli,[26] Jacobi[19] and Oberriether[27] describe methods which use hydrochloric or sulfuric acid and different indicators. These methods are principally similar to the alkali neutralization capacity method of Burckhardt.

Laube,[18] as well as Jacobi,[19] have found that soap and alkali detergents decrease the alkali neutralization capacity and increase the acid neutralization capacity of the skin. Neutral and slightly acid washing agents have, according to Laube,[18] practically no influence on these two functions of the skin.

Doubtless as important as the previously described physiological functions of the skin are the water content as well as the water holding and water absorbing capacity of the stratum corneum of the epidermis.

The water content of the stratum corneum, as Jacobi[28], Staras,[29] and Schneider and Schuleit[30] have shown, is necessary for a normal functioning of the epidermis. Blank[31] has confirmed these older European results in his very interesting studies on calluses.

Water Content of Skin

The study of the influence of detergents in regard to the water content of the stratum corneum is experimentally extremely difficult if the tests have to be performed on the living human skin and not on skin parts which have been removed from the body. Attempts have been made to measure the water content of this skin layer by employing the change in resistance of direct currents using needle electrodes inserted in the stratum corneum. In this method several factors cannot be sufficiently controlled, which may cause wrong results. For example, some of these factors are: The well known polarization of the direct currents, the differences in the thickness of the horny layer, which cannot be determined, and the inclusion of deeper layers than the horny layer in the determination by the creation of an electrical field by the current.

In studies not yet published we have developed a method which allows determination of the influence of all kinds of treatments on the water content of the horny layer of the living human skin. We carefully scrape the horny layer off untreated and differently treated skin areas with a sharp scalpel. The scrapings are separately collected in weighing bottles, immediately weighed and then dried to a constant weight and re-weighed. The difference in the weight before and after the drying represents the water content.

In their studies on calluses, Blank and Shappiró[32] have found that the treatment with soaps and detergents decrease the water content of the horny layer. The determination of the water content of the stratum corneum is very important according to Blank's results and ours, since a decreased water content of the stratum corneum parallels the decrease in the water holding and water absorbing capacity of this skin layer. On the other hand this is very likely connected with the occurrence of dry, rough, scaling skin by the use of detergents.

Skin Wettability

Also closely related to the water content of the stratum corneum is the wettability of the skin surface. The wettability can be measured by determining the wetting angle or, simpler, the spreading area of a water drop placed on the skin surface under certain conditions. In the performance of this experiment a drop of water falls on the skin surface from a calibrated pipette which is fixed at a given distance. For better visibility the water is colored with methylene blue.[28]

As our studies show,[33] the wettability of the skin surface decreases by treatment with water, soap, solutions of different inorganic and organic acids and furthermore with ammonia solution and different solvents.

The water content and the water absorption capacity as well as the wettability of the skin are strongly related to the presence of water-and polar solvent-soluble hygroscopic compounds in the cornified epidermis. We have proved that these compounds are re-

(*Continued from page 851*)

Packaging and Selling

"Best of the Year"
in the 1957 Aerosol Package Design Awards Contest, sponsored by the Aerosol Division of the Chemical Specialties Manufacturers Association, were Rexall Drug Company's "Stag" shave cream and Helena Rubinstein's "Five O'Clock" perfume mist. Both won first place in their individual product categories and were tied for "Best of the Year" honors.

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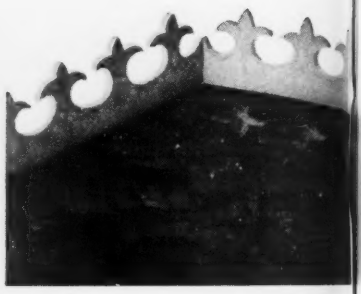

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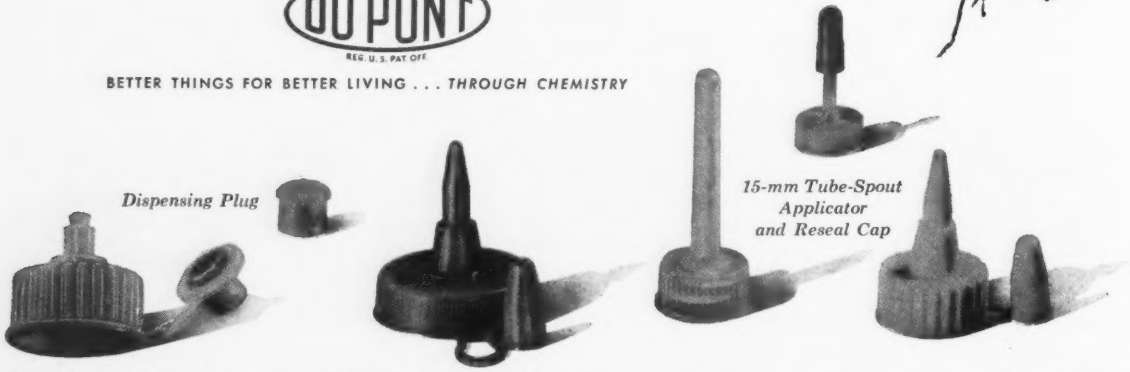

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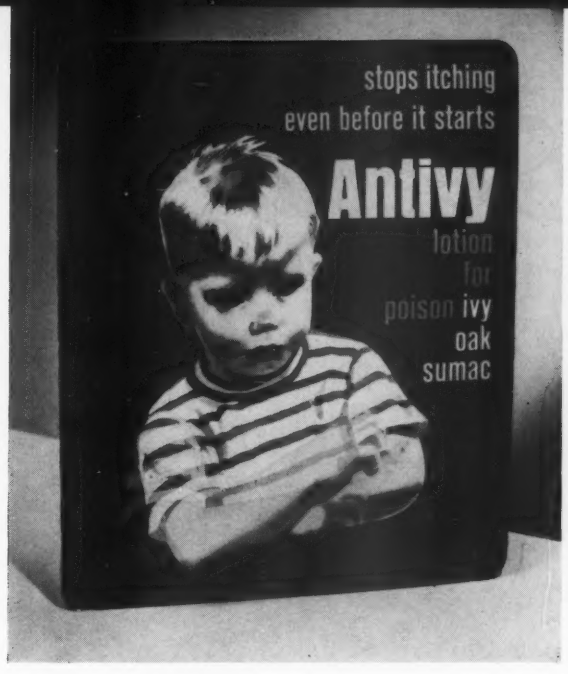

Merchandise Incentives

A PHARMACEUTICAL MARKETING TOOL

By DOUGLAS E. WARD, DIRECTOR OF MARKETING RESEARCH, CIBA PHARMACEUTICAL PRODUCTS INC.

Last Spring, when ready to market Antivy (Tripelennamine Hydrochloride USP And Zirconium Oxide Ciba) we were faced with the problem of getting the quickest possible distribution before the onset of the poison ivy season. The problem was doubly important, because Antivy, a new drug designed to prevent and control poison ivy, was to spearhead an intensive effort to win a share of the poison ivy preparation market. This meant that we had to compete with established ethical products plus many proprietary products.

Consequently, we decided to provide our men with an added incentive to insure their optimum sales effort coincidental with the product's introduction. We had successfully used merchandise incentive programs for the past four years. These campaigns have been aimed not only at our field representatives, but also at their families, who in turn encouraged their participant to compete for the many attractive prizes offered.

With the cooperation of our sales incentive agency, Cappel, MacDonald and Company, we mapped out the campaign structure. The Dayton, Ohio agency worked with us on the selection of a theme, "Over-The-Counter Sale Campaign," provided us with various visual materials, including an elaborate catalog which displays over 1400 items of merchandise.

When the incentive program ended three months later, the results far exceeded our expectations. As a result of our concentrated efforts, we soared 67 per cent over the anticipated sales.

This is how the campaign worked. As we analyzed the Antivy marketing picture, it was apparent that the successful introduction of the product would be contingent on accomplishing three main goals: Quick stocking of our product in drug stores; quantity distribution; and setting-up of special point-of-purchase displays.

To understand the significance of these achievements, it should be pointed out that in order to compete in this highly competitive poison ivy market, it was necessary for us to revise the traditional approach used to launch a prescription product and place increased emphasis on drug store activity.

Since the emphasis at Ciba is on prescription drugs, our field representatives concentrate their efforts on the physician. Because the success of an over-the-counter product depends in the main on the druggist, we had to get our salesman to alter his routine and do a more active selling job on the pharmacist.

The reasons we decided that the merchandise incentive plan would be the best way of getting our men to do a more aggressive selling job were several:

The infinite variety of prizes—ranging from utilitarian to luxury items—for the entire family. Here we have learned that these tangible awards serve to remind the salesman and family of his accomplishments long after the campaign ends. Psychologically too, merchandise awards seem more satisfying, since the salesman would ordinarily not feel justified in buying the prize had he the necessary money.

The great number of winners. Contrary to the usual sales contest, almost every one wins some kind of prize in a merchandise incentive program in direct proportion to his effort. In the Antivy campaign, where participation of field representatives was very

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Phone: GRanite 6-6311

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Phone: LEnox 2-3311

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435 S. LaCienega Blvd., Los Angeles 48, Calif.
Phone: BRadshaw 2-2995

COLONIAL APPLICATOR CO.
VINELAND, NEW JERSEY

high, 95 per cent of the men won prizes.

The opportunity to accumulate prize points from other campaigns. In a merchandise incentive campaign where prizes are awarded on the basis of the number of points earned, this is important, because the greater the number of points the more valuable the merchandize that can be selected by the participant. Cappel-MacDonald and Ciba worked out this arrangement to the satisfaction of our field representatives.

This last feature also provides a continuity of interest, builds up an increasing enthusiasm and increases morale. We have learned that the sales force responds positively when recognized by management for improving performance. As a result, we have found that each campaign brings out a larger number of participants and that the gap between the top winners and the runners-up in points accumulated is steadily lessened. In effect, this means that our field representatives have become more direct-sales conscious twelve months of the year. This year-round increase in performance has been substantiated by sales records.

There was another advantage to this type of campaign that concerned Ciba management more directly than the salesmen. This was the fact that we were able to stretch our award budget by about 50 per cent because we purchased the prize merchandise at an average discount of 33 1/3 per cent.

At our regular bi-monthly district meetings, the salesmen were told the story of the development of Antivy, were provided with promotional and point-of-sale display material and participated in discussions on the ways and means of merchandising the new, seasonal product in the quickest manner possible.

It was not difficult to stir up initial enthusiasm among our salesmen over Antivy, because it was quickly apparent to them that they had a unique product. Antivy lotion not only controls, but in most cases can prevent ivy, oak and sumac poisoning. It disappears completely when rubbed into the skin and does not leave any unsightly marks—a feature that would have great appeal among women.

Another factor that helped instill in our staff the confidence so important in launching a new O-T-C product was the attractive packaging. Realizing the importance of visual appeal to an over-the-counter product, we had packaged the Antivy in an eye-catching polyethylene, nonbreakable, squeeze-type red, white and blue container designed especially for counter display. This was one of the first moves in an overall program for repackaging non-prescription products.

In addition to a liberal supply of Antivy for distribution, our men also were supplied with such visual selling aids as a battery-driven motion display card showing a little boy busily scratching away at a poison ivy rash on his arm.

Our staff also had the advantage of being supported during the entire period of the campaign with publicity releases to the trade, general press and radio, plus advertising in trade publications.

Approximately 300 representatives, working from twenty-four districts, took part in the nationwide campaign, which ran from April 1 through June 30. Separate competitions were set up in each of the twenty-four districts. Quotas were established in this office but were reviewed and approved by the Ciba district managers.

The representatives had two areas in which they could work toward their quotas: direct sales to Ciba customers, that is drug stores; and turnover sales, taking orders from pharmacists who buy through wholesalers and turning these orders over to the wholesaler.

In each category, the salesman had to achieve 75 per cent of his quota before he could begin to accumulate points toward the merchandise prizes. That is, if the representative's quota was 50 dozen of Antivy, he did not earn any points until he had sold 37 1/2 dozen. Thereafter, for each one per cent of the quota sold, the representative received ten points, up to and including 99 per cent of quota. When the goal (100 per cent quota) was reached, the points doubled, and then for each one per cent sold over the quota, 40 additional points were awarded.

To keep representatives informed of the progress of the campaign, monthly letters were issued, giving individual and district standings. Each district manager and representative was furnished with a breakdown of the individual standings of all men in his district. Letters to salesmen also included the ratings of the national leaders. Our experience has shown that,

(Continued on page 850)

POWR-PAK, INC.

Proudly announces a history-making advance in pressure packaging...

INERT GAS PROPULSION

This highly significant new development permits the use of an inert gas as propellant to allow for the pressure packaging of many formulas not possible with present day fluorinated propellants.

Immediate inquiries are invited on:

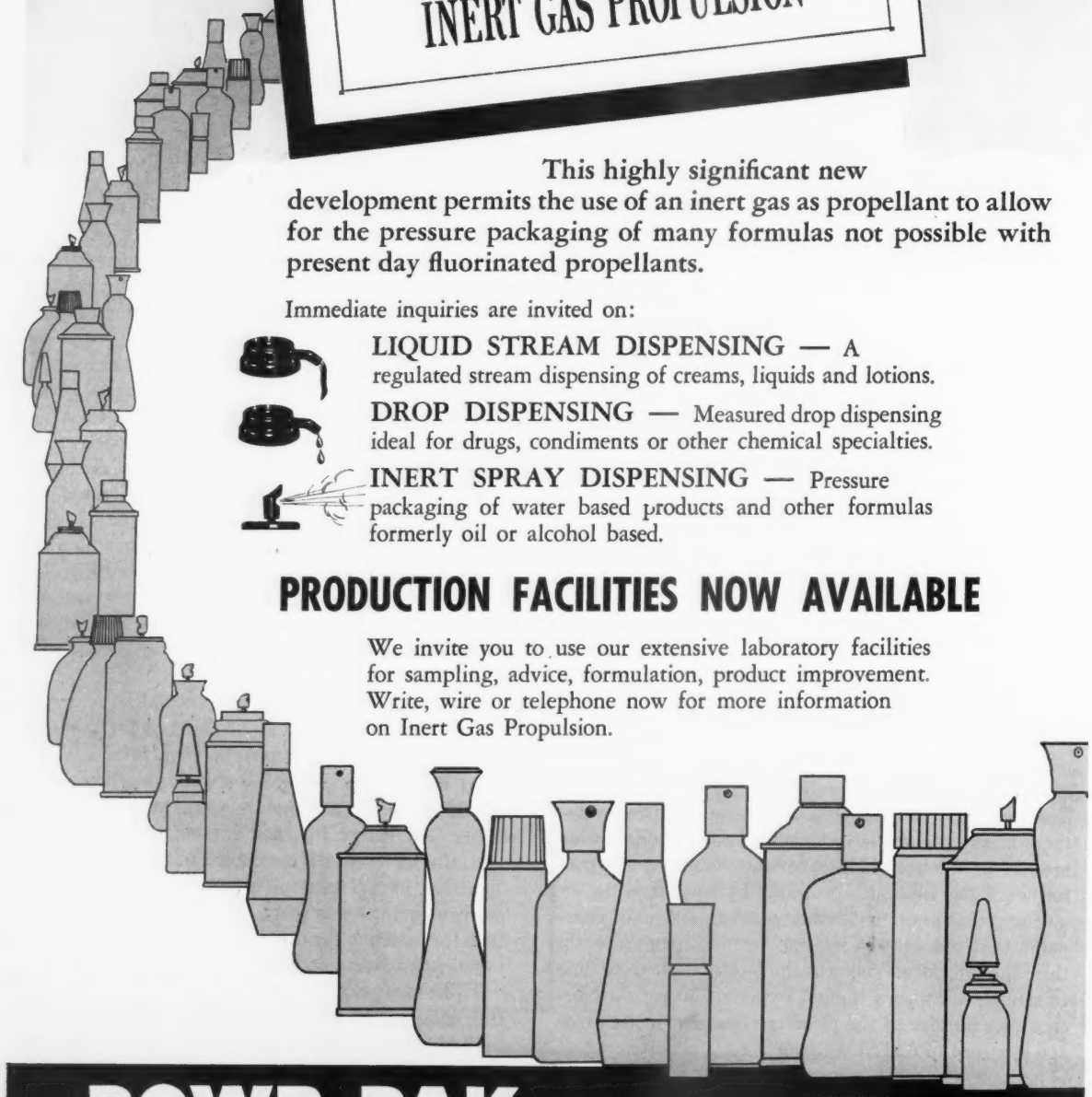
LIQUID STREAM DISPENSING — A regulated stream dispensing of creams, liquids and lotions.

DROP DISPENSING — Measured drop dispensing ideal for drugs, condiments or other chemical specialties.

INERT SPRAY DISPENSING — Pressure packaging of water based products and other formulas formerly oil or alcohol based.

PRODUCTION FACILITIES NOW AVAILABLE

We invite you to use our extensive laboratory facilities for sampling, advice, formulation, product improvement. Write, wire or telephone now for more information on Inert Gas Propulsion.



POWR-PAK, INC.

643 North Avenue, Bridgeport, Conn. FOrest 7-6495

Package Development

By GEORGE J. SCHLECK, MANAGER OF PACKAGE DEVELOPMENT, MERCK & CO., INC., RAHWAY, N. J.

In any analysis or discussion of such a broad subject as organization for package development, I believe, it is well to first analyze what is it, you want to organize. Let's move back a bit and define the forest we are working in before we chip away at the trees. Let's analyze those factors, functions, or elements that comprise package development and broadly define these factors in terms of more familiar existing organizational patterns.

Packaging Materials?

The first in this series of elements that go to make package development is the knowledge of packaging materials. Knowledge of bottles, cans, corrugated, plastics, films and foils, liner materials, box board, etc., is the nub of package development. We must know what their good points are, and what their weak points are.

Product Research?

Our next factor of concern is the product itself. What are we trying to package, what is the form of the product—liquid, solid or gas, what are the product characteristics? Is it a sterile product, is it affected by atmospheric conditions particularly in the food, chemical, and drug industry, problems of decomposition, spoilage, compatibility of the product and its container? These plus a host of other pieces of information characteristic of the product is a factor in package development. In other words you must know your product thoroughly in order to package it properly.

Marketing

How is the product to be used, where is it used, what is it used for, what is the proper quantity to be packaged in terms of a unit, are special gimmicks needed—such as adapters, pouring spouts, etc. to use it properly? What does our competition do, what's the price range of the product, are there any specific trade market preferences or traditions, what about market testing? This type of data is the normal concern of a marketing department.

Purchasing

In selecting the type of container what types are available, their cost, is it a stock item or must it be made special, who are the suppliers, what is their reliability, what quality can we expect, where are the suppliers located, what services do they render, what about alternate sources of supply, what are the market conditions? Now our package development is taking on the airs of the purchasing function.

Production - Engineering

Now that we have the product and the package, theoretically how will it be put together or how will it be packaged, what equipment is required, is the equipment available or must we design new equipment or purchase new equipment, are special methods or jigs required to package the product in our selected container, do we have sufficient production time, what is the speed of the line and what are our manpower requirements, are special skills needed? In this phase of package development we have a production or engineer hat on.

Quality Control

How can the commercial tolerances of our completed packaging material be maintained—incoming supplies, inspection, what can we expect during production or field performances, shelf life, machinabil-

ity, etc.? We are now concerned with quality control.

Warehousing and Shipping

What's the proper case size, are we concerned with palletization, how will it be shipped—truck, car load, parcel post, are we concerned with I.C.C. and C.F.C. regulations, what are the handling problems between packaging to delivery in the hands of the customer, what degree of protection must we have? What about breakage problems? These are the functions normally concerned in warehousing or shipping.

Promotion - Design

Up to this point we have discussed primarily physical problems of package development, however, our functions are not complete. We now have consideration of consumer appeal or consumer acceptance, point of purchase displays where we are concerned with the style, color, and type of package label and display from its aesthetic and in many cases functional viewpoints. You might term this phase of package development as design or promotion.

Legal

Now our theoretical package development man must also be concerned with F & D A, Bureau of Agriculture, and other government agencies, patent problems, trademarks, and advertising claims. Now we are a vest-pocket lawyer.

Accounting

The last of our broad functions of package development, but by no means the least is cost. Labor, cost, overhead, distribution, freight rates, etc. must all be accounted for and analyzed. Let's call this Accounting.

I don't mean to imply that we have covered all the factors here, and you may disagree with some of my headings; there may be other factors peculiar to your products. However, generally speaking, these are all of the considerations and all of the elements that must be accounted for, correlated, and integrated into the single package. All of these functions with their many and varied ramifications must be included, considered, and rectified in the development of a finished package.

You will note from this that on the theoretical basis package development is not the prerogative of any one organizational area but is of concern and is truly the integration of elements of all organizational functions.

In the broad analysis we have determined what constitutes package development. Now let's turn it around and look at package development in terms of our particular requirements. From here on out the pattern of package development varies considerably. No two organizations requirements are the same. There is no standard pattern for organization and each company has to build its package development function to fit its particular needs and the needs of the company as a whole.

The type and scope of a package development organization must now be analysed in terms of (1) the products sold or the type of market we are working in, (2) the company philosophy, policy or climate in relationship to Package Development, (3) the calibre, ability, and stature of the people in the organization and (4) the strength and the quality of these existing related functions. With these four points firmly in mind the problem now is to analyze each of the base elements and determine its *relative importance* to the overall packaging effort.

The type of product, the type of market will in most cases predict the important elements of package development. Once we have analyzed and ranked the important elements, let us examine our existing organization to see what is available. Are these functions being done, how well are they being done, (I refer to their relationship to packaging problems) and is the information available in a form that can be easily digested? At this point our weak spots will start to become apparent.

Throughout this analysis, a strong word of caution. This is not a check list to be marked off with a pencil, but a depth analysis based on not only what we are doing but how well we want to do it and how deep or how thorough a job is required.

Once we have determined our needs and have gone through this analysis, a pretty good framework of what our organization should be will start to become apparent. The number of products or degree of activity, the importance of related functions, the climatic conditions of the company, the ease of communication will start to indicate how large a package development organization is required. It could be a single individual with broad enough stature to coordinate and give direction to the elements already established. This is particularly true if only a few products are involved. However, as products become more numerous and the amount of total activity increases, combining all of the controlling elements into one department may be preferable in order to give ease of flexibility and to coordinate and give direction more effectively. I believe that probably the most practical approach is the combination of the two. Combine the natural and controlling functions together under direct supervision and coordinate from there other necessary elements. This provides greater flexability and acts as focal point for data and information.

In summation, a package development organization is not a rigidly cast function. It employs all of the elements within the normal compliance of a company but varies to its degree of importance. Last, the package development function must be tailored to fit a company, its market, its philosophy, and its goals.

glass containers move more drug products

Use **Anchorglass**® *containers sealed with* Anchor® *caps*

...because they are preferred by housewives

HOUSEWIVES recognize the glass container as the most sanitary package. They prefer glass because it effectively protects the purity, strength and other qualities of the contents until entirely dispensed . . . does not rust or corrode . . . is chemically inert . . . prevents evaporation, leakage or moisture absorption. And they prefer glass containers for ease of opening and resealing. Take advantage of this decided preference—pack and move more of your products in glass . . . in Anchorglass containers sealed with dependable Anchor metal or molded closures.

ANCHOR HOCKING

GLASS CORPORATION

Lancaster, Ohio

Packaging and Selling

Packaging Toothpaste

The ever restless toothpaste business is big business, not only in this but in any industry. Substantially topping $160,000,000 of the public's money each year it provides a very juicy plumb enticing big business to shoulder its way into this market or to fight valiently and desperately for a top position.

Toothpaste is one of the most saturated markets in American industry. It is a fixed daily habit of a vast majority of American people, men, women and children. For all of these reasons it would be expected that in this turbulent, competitive American market that toothpaste marketing would have all of the evils and hazards of American competition as well as all of its advantages.

Not too long ago, that is in the rather placid days between the two great world wars, there was a rather rigid brand loyalty for toothpaste and the well established dentifrice manufacturers had no competitive problem except to keep an even course on a well established marketing formula. Since the Second World War, however, toothpaste has joined the ranks of those products which command only a feeble and a fluctuating brand loyalty by the public.

Because of this very vulnerable brand loyalty, we have seen in the last ten years a continued succession of so-called therapeutic miracles each in turn a seven months wonder and each bringing temporary turbulence into the market and affecting the market position of the toothpaste brands.

During the last few years there has been a period of relative peace in the toothpaste industry. This may be because the American public and the retailer have soured on this ever recurring therapeutic miracle or because the laboratories of the dentifrice companies have failed to come up with something sufficiently stimulating from an advertising viewpoint.

Apparently a market as big as $160,000,000 a year plus is just too much for continued peace. So, it would seem, the manufacturers in this industry, at a loss for another therapeutic miracle, have turned to that other basic device for introducing a new cosmetic product or giving a tremendous sales impetus to an established one—that is, a new device, principle or gimmick in packaging.

Bristol-Myers appears to be a leader or at least one of the first in this new phase of toothpaste competition. According to reports current in the trade, the new plastic squeeze bottles for Ipana are not only rolling up sales for the toothpaste but are opening new vistas in this type of container for cream or paste products.

This new plastic container is said to be introducing a nice new element into the toothpaste business, that is it is proving that buyers are willing to invest a little more capital for a substantially larger amount of the product. Ipana, in the plastic container, is advertised as "Outlasting three giant size tubes." In this preliminary stage an interesting part of the public seems to like this idea.

Not to be outdone in this new era of toothpaste packaging competition, we understand that Colgate has completed all of its research in an aerosol toothpaste package and is now marketing this package, the first application of Aerosol to toothpaste dispensing so far as we know.

We have not seen this new reported aerosol toothpaste package of Colgate but trade reports say that it lays a fine even ribbon of toothpaste on the brush in the best traditional manner of toothpaste application.

Once the competition in an industry or in a product field switches over into such a new development as packaging and dispensing, almost anything can happen, because packaging is a huge, versatile and varied industry with a great many creative minds working on a large variety of packages and dispensing devices.

In a recent issue we cited a report about the Lampar Company of Dallas which, according to our information, is now marketing a toothpaste in tablet form in test markets in the southwest.

Toothpaste has been one of the stablest markets in form and package in our industry for very many years. Except for a modest venture into liquid toothpaste and a few years period where powder commanded some attention, the dentifrice market has been predominantly a paste or cream entirely committed to one package, that is the collapsible tube.

It is extremely interesting to notice that the two toothpaste giants, that is Bristol-Myers and Colgate have in the past, for many years, each been intimately associated with collapsible tube manufacturing company. In the case of Bristol-Myers, this was until very recently the outright ownership of Sun Tube Company, a collapsible tube manufacturer.

Whatever may happen in the toothpaste business, these aggressive companies controlling many millions of dollars in advertising will undoubtedly put on a very interesting show in the next few years. Packaging people will watch with deep interest this highly competitive race which, at the present time, is basically

If You Sell from a Grab bag...

. . . then you've really got the packaging problem licked. When the customer reaches blindly in, she's stuck with whatever her hand pulls out of the bag. Maybe that's why grab-bag sales have shown a notable tendency to decrease in recent years.

Fortunately for everyone, most sales today are made in brilliantly lighted stores, with the customer making her choice from well-displayed groupings of competitive products. She has plenty of time to select the brand that will best satisfy every wish she has for that product.

Imco squeeze bottles add use appeal . . . safety appeal . . . and eye appeal to every product they contain. So to pull your product out of the grab-bag class and into the choice class of present day merchandising . . . let Imco help you design a container that will fit your needs at the point of sale . . . and in use.

IMCO BOTTLES CARRY FLEXCEL THIS TRADEMARK

IMCO CONTAINER CORPORATION

Empire State Building, Room 6204
350 5th Ave. New York, N.Y.

27-67 Vine Avenue
Toronto, Ontario, Canada

75th & Cleveland
Kansas City, Mo.

Palmolive Bldg., 919 N. Michigan Ave.
Chicago, Illinois

608 McCall Bldg.
Memphis, Tenn.

4515 Olive St.
St. Louis, Mo.

5957 South Western Ave.
Los Angeles, Calif.

Just grip—bend—snap! Kimble COLOR-BREAK Ampuls are ready to use. No filing, sawing, scoring. Kimble Multiple Dose Containers and Kimble Syringe Cartridges, available in wide range of capacities.

Your injectables deserve Kimble-quality packaging protection . . .

PERFECT CONTAINER protection is an absolute "must" for serums, drugs and other life-saving solutions.

When you package in famous Kimble containers, you can be sure that your parenterals will maintain utmost purity, consistent potency. For Kimble containers cannot contaminate or alter the effectiveness of their contents. Here's why:

To assure top-quality protection, Kimble Neutraglas bottles, syringe cartridges and COLOR-BREAK® Ampuls are made of a special-formula borosilicate glass which has the highest resistance to chemical attack of any known "workable" glass.

For detailed information, sizes and prices of Kimble's complete family of containers, write Kimble Glass Company, subsidiary of Owens-Illinois, Toledo 1, Ohio.

KIMBLE NEUTRAGLAS CONTAINERS
AN (O) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES • TOLEDO 1, OHIO

committed to a collapsible tube, a plastic bottle and a tin aerosol can.

No Thanks

We have been invited to try about everything by the tooth paste people except the newest brand which is offering the consumer genuine scotch and bourbon flavored tooth paste. If you like this, the same outfit will sell you bourbon and scotch mouthwash.

Again Kudos to BRECK!

We have many times in this department commented on the fact that the Breck advertising is probably the most widely discussed current advertising in our entire industry, if not in the entire field of advertising. This advertising has always been interesting to us, not only because we can claim some degree of friendship with the people who are both creating this advertising and also okaying it.

Brecks advertising is also essentially interesting because in many ways it has violated many of the traditional convictions in professional advertising circles. For instance, a recent article in Printers' Ink quoted the opinions of several advertising men that Breck advertising was old fashioned, bad selling and other far from favorable comments.

Now we find another article which we feel compelled to quote. This is from that extremely intelligent and highly interesting column of Kenneth Collins which appears every day in Women's Wear. A great many of our readers who never see Women's Wear should remember Kenneth Collins as one of the outstanding retail advertising men of the last decade. Here is what he says.

"I just cannot keep my eyes off the Breck Shampoo advertising. I know no one in the company and have asked nobody about the acceptance of the product. But if it is not high, I shall cash in my typewriter and concede that a lifetime spent in sales promotion has been wasted. For this campaign has everything.

"Year after year, the women of America have seen the heads of lovely girls who, by suggestion, rather than by some huckster's shouting, owe much of their good looks to this hair preparation. The format appears not to have altered over this entire period. The magazines used and the preferred positions obtained, seem not to have varied. The container has been prominently but not unpleasingly pictured. The copy has made no extravagant claims. The differentiation of types of shampoo for dry, oily or normal hair impresses one as within the usual experience of customers.

"But the astonishing central fact about this campaign has been its extraordinary consistency. In a publicity world in which most people are forever hell-bent on making change merely for the sake of change (and frequently for no other conceivable reason) some person in Breck has kept this advertising unswervingly on the track. We are all familiar with the postal department's motto: "Neither snow nor rain or heat nor gloom of night stays these couriers from the swift completion of their appointed rounds." How I wish some paraphrase of this could be written for and followed by the advertising business. For once a fine concept is worked out, how desperately this craft needs a classic admonition to keep unwaveringly at the job.

"Breck has done this. What a lesson for stores! What a lesson for all advertisers! Millions of soundly conceived ads are run every year. But how few—how pathetically few—are ever followed up. In retailing one thinks of Tiffany's brilliant little series, A & S's amusing copy and illustrations about complete assortments—but the list, regrettably, is short. So cumulative values are lost; the waste of money that follows is deplorable.

"And now one notes that Breck, with its package handsomely bedecked for the holiday, is about to cash in for Christmas. I hope the company's volume sets a new record. And to whatever executive it is who has had the vision to plan such beautiful advertising and the courage to live with it, I send my earliest and heartiest good wishes for the coming season."

Saving Barbasol

How bad can a product be and still keep selling and still keep justifying advertising expenditures?

According to William Tirrell, vp in charge of advertising and marketing of Barbasol Company, in a speech before the American Marketing Association, it can get pretty bad. As a matter of fact, according to Mr. Tirrell, it can hardly have been worse.

To quote, "Consumer tests show that there was considerable evidence that Barbasol Presto lather was too thin, not quite as pleasant on the skin, and that it dried too quickly.

"I say this rather casually but there really is not much more that could be wrong with the lather.

"Our dispensing system—the dispenser for ejecting lather—was inferior to that used on Rapid Shave.

"Finally the study also showed that the cap that we used on the Barbasol tube was less acceptable than the competitor's cap."

All these things have now been corrected which we would venture to say is an attribute to the practicability of consumer research.

Big Advertising

Advertising is a necessary method of sales and communication in order to build up a mass market. Just what part of advertising, however, is used exclusively for competitive purposes and for market domination are subjects that were seriously discussed in the early '20's and probably will be discussed even more seriously some day soon.

As an example of big advertising, Printers' Ink has just released some figures which shows that last year Procter & Gamble spent $55,477,411. This was a rise of more than $13,000,000 from 1955, enough to edge General Motors out of first place. In the preceding year G. M. had edged out P. G. but in 1956 G. M. spent $48,981,798, up more than $4,500,000 from 1955.

In third place was Colgate-Palmolive with $29,566,-513.

A Big, New Problem in Retailing

For several years now there has been an increasingly enthusiastic or bitter debate, according to which side you are on, over night hours for retailing.

There have been many reasons why this trend toward night retailing has been taking place, particularly in the supermarkets and to a certain extent in

EXCITEMENT!

that's the word for
Wrisley's
new, crystal-clear
Gaiety Bubble Bath packages
by CELLU-CRAFT

FIRST AWARD!
1957 NATIONAL FLEXIBLE PACKAGING COMPETITION
Pharmaceuticals, Drugs, Cosmetics & Chemicals Classification.

PROBLEM: WRISLEY needed a package that would: a) protect the fragrance and texture of its bubble bath powder; and, b) sparkle with eye-attracting sales appeal.

SOLUTION: Call in Cellu-Craft to develop the package.

RESULT: Excellent protection of product achieved by careful selection and treatment of the proper film. *Permanently* sparkling colors were achieved with special inks, specially treated.

RECOMMENDED: You're in the best company when you put Cellu-Craft package development engineers to work for your firm . . . your products . . . and watch sales grow.

CELLU-CRAFT
PRODUCTS CORPORATION

Designers, Converters and Color Printers of Flexible Packaging Materials

General Offices & Plant: **1401 4th AVE., NEW HYDE PARK, N.Y., PRIMROSE 5-8000** *Sales Offices in principal cities*

PRINTED CELLOPHANE • POLYETHYLENE • PLIOFILM • FOIL • ACETATE • in ROLLS • BAGS • POUCHES • ENVELOPES • SHEETS

metropolitan department stores. This movement does not seem to have penetrated to the small specialized retailers in other fields and to the service stores to any great extent.

Nevertheless, it has been stated by many people over the last several years that retail store hours have been adjusted to the convenience of store personnel and less and less to the convenience of the store's customers.

The Grey Advertising Agency in their last retail edition "Grey Matter" covered this subject thoroughly and completely in an analysis which gives 16 reasons why night hours are inevitable for retail stores. Some of these reasons, such as easier traffic conditions at night, almost total dependence on the family car as a shopping vehicle and the trend to shopping as a family unit are among the 16 reasons.

There is no question that the general employment of women in this country today and the fact that in a high percentage of families the man must take the family car out of circulation each day in order to go to work, has been bringing a substantial social change which must have its effect on retail shopping hours.

It seems to us that there is still another vital consideration for retailers, especially for the big powerful retailers such as supermarkets or department stores, which tend to dominate a community and particularly to dominate suburban shopping centers.

These large institutions, with potent ability to attract traffic, have been enormously increasing their capital investment, not only in inventory but in real estate and in physical properties. There certainly is a very compelling reason for getting the utmost out of this capital investment and if these stores can expand the productiveness of this capital investment from 8 to 12 or 14 or more hours and maintain substantial traffic during that increased period, then there is certainly a potent arithmetical reason for them to prolong opening hours.

There is unquestionably an increased desire to do more night shopping in this country. In addition to the fact, as mentioned above, we think there is a growing inclination on the part of American families to shop together for reasons of taste, of economics and for the blunt necessity of carrying heavy packages. We sometimes tend to forget that self-service has imposed a very heavy physical burden on the woman customer in compelling her to take care of the freight delivery as well as the buying.

If night openings become an important development in this country during our present retail revolution, the big and enormous question which retailing must then face is this: Would we then have far too many retailers and is our retail physical capacity enormously over expanded? Certainly if a supermarket operates 12 hours instead of 8 hours, we may have a store and a half in this single unit because of that extra time open for shopping.

Remember the Retailer

It seems to us, as we read the Business Press, that an increasing number of major advertisers are beginning to think of the retailer, not as an automaton, but as a human being increasingly important in his distribution.

The outgoing chairman of the Association of National Advertisers, George Mosley, who is also VP in charge of advertising and sales promotion for Seagram's had this to say:

"I believe that what happens after an ad appears is just as important as what happens to make it appear. Respect the retailer, for he can siphon off the power of any ad campaign in the world, if he wants to. Get out there and see this other power in the marketing cycle at work, and see how to make your advertising more understandable and therefore more merchandisable, to him."

May be the period of complete abdication by the retailer for all selling functions is disappearing. The return of strenuous local competition is forcing the retailer to awake to his own responsibility for creative merchandising in his community. At the same time, it would seem that the manufacturer is finding out that it is not always to his advantage to think of the retailer in terms of a faceless puppet for which he pulls the strings with his advertising.

Minnesota Survey

Minnesota Homemaker No. 9, a new study in the "Continuing Survey of Minnesota Living" conducted by the research department of the Minneapolis Star and Tribune is now available. This is a market survey of a wide variety of products in our trade. In addition to brand position, it gives the percentage sales from 1953 through 1957 and the relative percentage sales of each of these products in cities and in town and rural areas.

Memory

Here's what you are up against when you spend some money on advertising. It is a study of training programs by the lecture system, but these results certainly apply to any form of human communication including radio, television and the printed word.

In a paper by an executive of the Minneapolis-Honeywell Regulator Company on sales training, here's what they found—

"If you listen attentively to a lecture, you will remember 10 per cent of what you hear.

"Three months later you will have forgotten 70 per cent of the 10 per cent."

Puzzles in Marketing

Here are a few cosmetic market problems that puzzle us. According to a compilation of a great many consumer surveys of cosmetics, a substantial number of cosmetic products, such as face creams, have shown declining sales and a declining percentage of consumer usage. Other classifications, such as make-up, have held a relatively static position over the last ten years with very little growth. A fact that must be recognized here, of course, is that such products as lipstick and face powder, have reached a high saturation point at the beginning of this period.

Certain other cosmetics, notably hair products and deodorants, have had a dynamic growth.

What puzzles us is that a high and growing amount of advertising in this industry has been spent for products showing a declining sale or a static sale. For instance, it is our opinion that the millions of dollars

OPAL . . . the aristocrat of glass
For beauty, utility and all-around satisfaction, opal jars are the most desirable containers for cosmetic creams.
Carr-Lowrey brings you opal jars at their best. Decorated with your own attractive design, they are outstanding containers for your finest products.
GLASS STIMULATES SALES
Cleansing Cream
CARR-LOWREY GLASS CO.
Designers and manufacturers of fine glass containers
Factory and Main Office: BALTIMORE 3, MD. • New York Office: 415 MADISON AVE. • Chicago Office: 1572 MERCHANDISE MART

spent for lip stick advertising in the last four or five years has not contributed in any appreciable way to a market expansion.

If we may accept the words of the fragrance people themselves, the fragrance advertising which ran to quite a few million dollars in the last few years has not contributed to any growth in fragrance usage.

In other words, just considering this one industry alone, we do not think that there is any evidence on the record, except in the field of hair goods and a few specialty products, that advertising has been contributing to the expanding use of the industry's products.

Another thing that puzzles us in cosmetic marketing is that during this entire era when a large part of the retail trade is abandoning personal selling and when many manufacturers believe that personal selling at the point of sale has become obsolete, that this should be a period of dynamic growth in house-to-house selling which is purely personal selling at the point of sale.

Still another factor that puzzles us is that during this era of multi-million dollar advertising where we hear so much about the consumer franchise which manufacturers are acquiring and where it is generally agreed that manufacturers are more and more taking over the functions of retail selling, that during this period in many retail fields there should be such a substantial growth in the retail owned private brand.

"New Concept" Drug Store

The Sun Ray Drug Company has just announced plans for the biggest expansion program in its 31 year history. Harry Sylk, president of the 160 drug store company, announced that 45 new drug supermarkets would be opened in the next fifteen months. According to Mr. Sylk, "a new concept" is on the way in the retail drug business. These new stores will be all-inclusive one stop shoppers centers.

In reading about this new retail drug store development, we cannot quite figure out whether the expansion is horizontal, vertical or tangential. Apparently these stores are getting ready to sell about anything the housewife wants.

In addition to the basic drugs, drug products, cosmetics, toiletries, the store contains a pet shop complete with tropical fish, tropical birds, live monkeys, parakeets, puppies, a line of pet foods, sporting goods, house furnishings, electrical appliances, hobby and craft materials, books, a complete record department, radios, refrigerators. The Queen's store also sells frozen and some exotic and rare canned foods, candy, clothing, sportswear.

Reverse

In a sort of reversed move of what is generally taking place, Snyder's drug stores are dropping half a million dollars annual volume in their food departments by either eliminating these departments entirely or drastically cutting them back in the larger stores. According to a chain executive, "We needed this food space for more of our traditional drug store merchandise and the food departments had to give way."

We expect to see the day when some of the major food chains will apply this same thought of logical thinking to their own stores.

Medical and Personal Care Survey

We seldom feel impelled to give any mention to the surveys which flow in a steady stream from the research departments of consumer magazines.

However, it appears that the current nation wide survey by Life Magazine does merit some attention.

According to this publication, the only comparable survey in depth and scope was that undertaken in 1950 by the Bureau of Labor Statistics. In the Life survey a nation-wide sample of 24,112 individuals in 10,243 homes were interviewed, each household at an average of eight hours.

Here are some of the conclusions in the classification "medical and personal care."

The best customers for cosmetics and beauty aids are families headed by a business executive in his 40's whose children are ten to nineteen years old and who lives in a northeastern or western big city or suburb.

The average U. S. family which spent a total of $1,110 in 1956 on all consumer goods and services spent $222 in the classification "medical and personal care" ranking this division seventh after the following divisions, food, home operation and improvement, automotive, clothing, home furnishings, equipment and appliances, and miscellaneous.

The average household in 1956 spent $11 on cosmetics and beauty aids. This compares to $50 on drugs and remedies, $5 on medical equipment and supplies, $6 on shaving supplies and equipment.

Medical and personal care count for about 5 per cent of the spending of the average household. The amount spent rises with income but not in direct step with it.

Of all the money spent by U. S. households on cosmetics and beauty aids in 1956, 22 per cent were spent by households with income under $3,000, 31 per cent was spent by households with income between $3,000 and $5,000, 38 per cent was spent by households with income between $5,000 and $10,000 and 9 per cent was spent by households with incomes of $10,000 or more.

Households in all the nation's geographical regions spent very nearly the same amount for cosmetics and beauty aids. The Northeast and West lead with $12. The South follows with $11. Right behind is the central region with $10.

There is no appreciable difference in spending as between big cities and their suburbs. In both, average 1956 expenditures were $14. In central city areas with less than a half million population and their suburbs, the respective figures are $13 and $10.

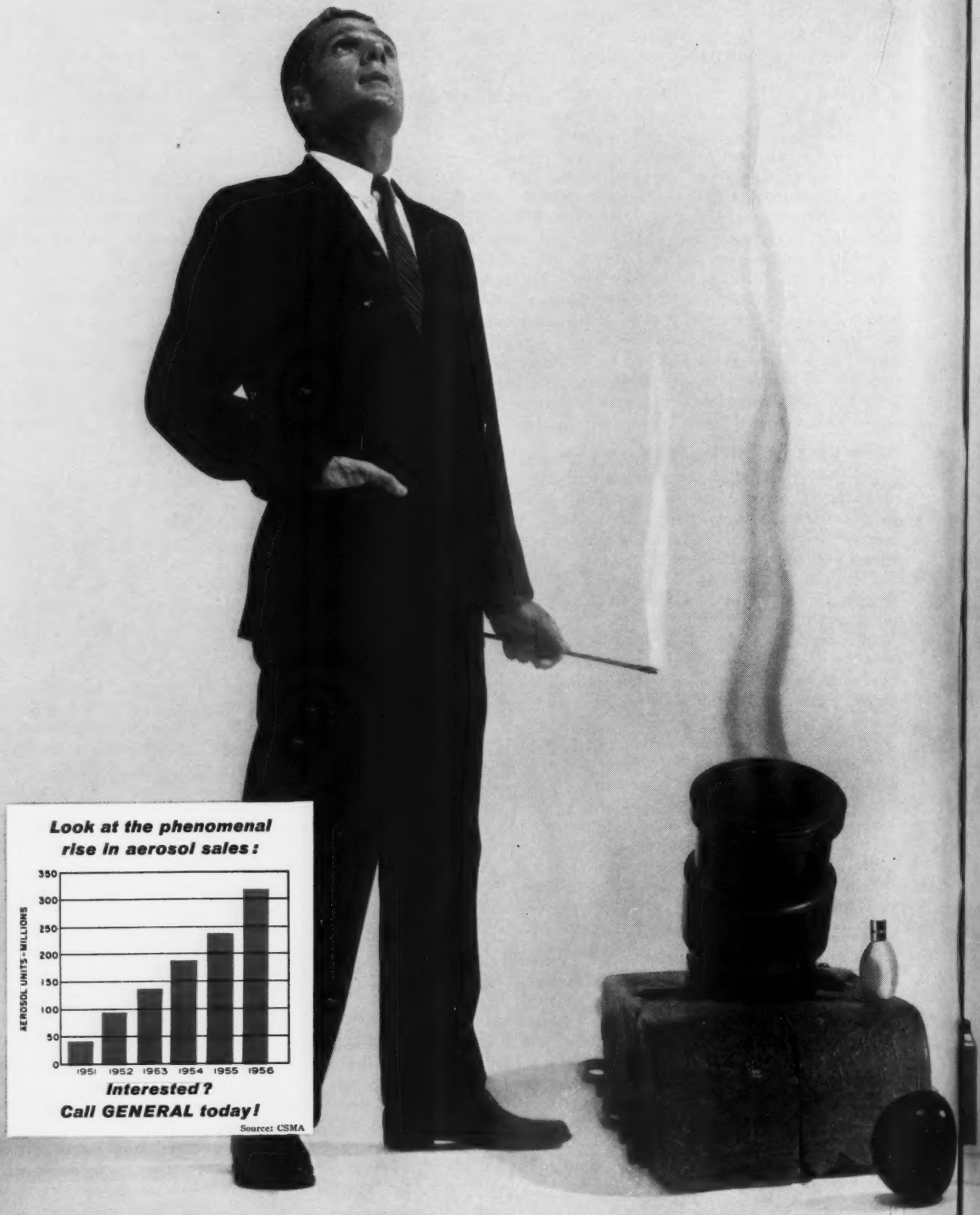
Education does not appear to have much bearing on spending for cosmetics and beauty aids. Among occupation groups, the largest expenditures for these products are made by households headed by business executives. Average 1956 expenditures for this group were $15. The sales-clerical and craftsman-foreman groups follow with average expenditures of $13.

Not Proud

This industry has the very doubtful honor of being among the top leaders in complaints and inquiries received by the National Better Business Bureau.

According to a recent report of the bureau, it is receiving four times as many inquiries concerning drug and cosmetic products advertising as it did two years ago "and, lamentably, ten times as many complaints."

AEROSOL



Look at the phenomenal rise in aerosol sales:

Interested?

Call GENERAL today!

Source: CSMA

PACKAGING

can start sales shooting straight up *for you!*

Had your eye on aerosols? Then you've seen sales shoot from 40 million units in 1951 to 320 million units in 1956. Aerosol sales have shown a steady increase of about 30% every year since '51!

Here's how *you* can get into this dynamic, high-profit field practically overnight—*without* heavy capital investment!

If your product can be sprayed, brushed on, dusted or daubed, it's a likely candidate for aerosol packaging. General Chemical will help you develop a formulation with the right pressures and compatibilities for your product and container. *No cost or obligation!* And there are many capable contract fillers throughout the country who will put up your product in aerosol form for test marketing, and handle commercial production afterwards. You do not have to invest in plant, special equipment or personnel to get into aerosols!

To arrange for a special presentation, write or call "Genetron" Department, General Chemical Division, Allied Chemical & Dye Corporation, 40 Rector Street, New York 6, N. Y.

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aerosol propellants

GC Allied Chemical

The Right Propellant for Every Aerosol Need!

Call on General for:

Free fact-packed technical manuals, market information

A complete aerosol research and development laboratory

Data on many promising new types of aerosols

Field assistance with propellant storage, handling

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40 Rector Street, N. Y. 6, N. Y.

Patent thoughts and trends

By THOMAS CIFELLI, JR., PATENT ATTORNEY*

Sputniks and Patents

The normal quota of patents has been issued since the last appearance of This Journal; but, nevertheless, the orbiting of the Russian satellites, in the writer's opinion, is the most significant patent news at this time. Consequently, a little thought will be given to the patent consequences of Sputniks I and II.

The reader may well question whether there is any connection at all between patents and sputniks. All recognize that a new look at the place of scientists in the society is called for. Already the President of the U.S.A. has taken what appear to be serious steps to try to bring the western world up to par with the Russians in the field of unmanned objects. Also, steps are doubtless underway to overhaul the system concerning the education of future scientists. In this connection, perhaps, we shall hear no more of the only three so-called "learned" professions: the law, medicine, and the clergy. Without in any way minimizing the contributions of these three professions, one can accept the fact that there should be no such limitation. The writer recalls once having listened to a very eloquent professor of law who gave what he considered to be the underlying reason for there being only three learned professions. His reason was that Man's three highest attributes are his rights (which are the concern of law), his body (which is the concern of medicine) and his soul (which is the concern of the clergy). It did not occur to the professor that the scientists, or anyone else who is concerned with the very survival of civilization, merit the appellation of being members of a learned profession.

Since we all are concerned with the survival of the human species, it behooves us all to ask ourselves whether we are individually and collectively meeting our obligations. For the present we shall consider this question from the point of view of patents. Perhaps a good way to start is to list the main groups who are especially interested in the day-to-day operation of the patent system. These groups are as follows:

1. The inventors
2. The investors
3. The patent attorneys and agents
4. The patent office
5. Congress
6. The courts

It is believed that by and large each of the groups does a workman-like job, from the point of view of its own narrow objectives. Thus, it cannot be gainsaid that inventors are still with us and producing new ideas. However, surveys show that the per capita output of American inventors, as measured by U.S. patent applications filed, has been on a downward trend for almost 40 years. In fact the output has been reduced by about 50 per cent. It would seem that the inventors particularly would be interested in finding reasons for this decline, in their own self-interest.

While it is understood that meritorious inventions always seem to find a financial backer, it is believed that the costs of procuring patents have gone up at a higher rate than can be accounted for by cost of living, etc. What the reason is would seem to be a particular concern of the investor group.

The next group, the patent attorneys and agents, come in contact with all of the other groups and therefore would appear to be in a peculiarly advantageous position to ferret out weaknesses and to suggest improvements. It is known that this group is very busy and perhaps for this reason has not considered important broad questions, but has had all it can do to consider the urgent narrow problems crying for solution, that is, the jobs at hand. Perhaps, however the very fact that just about all patent attorneys and agents are extremely busy should in itself give pause for thought. Is the crush of work accompanied by greater productivity or is it in good part due to the fact that there are so many rules and considerations to be kept in mind in preparing patent applications that the job of preparing *a* patent application today takes up a lot more time then it did, say 30 years ago? If the answer is the latter, why should it take longer?

The Patent Office is the governmental arm which is most intimately connected with the patent system. Commissioner of Patents after Commissioner of Patents has pointed out the huge backlog of patent applications. This is so even though the per capita output of patent applications is only 50 per cent of what it was about 40 years ago, as already noted. Fees payable by patent applicants and salaries of Patent Office personnel have been increased. Many other things have been done to try to improve the situation. However, is it possible that there is an untapped area where great improvement can be made? Is there any reason, for example, why concepts which were justified during the 19th century should still be considered binding? Is everything possible being done to eliminate time-consuming rejections based on trivial grounds. In this connection, is the word "or" really such a bad word that it should not be permitted in patent claims? Also, is it really so that a negative limitation such as "without" is any less definite than "in the absence of"? One often is tempted to question what the results of a motivational research study of the Patent Office personnel would show as regards their broad attitudes. For example, do Examiners really believe they are cast as *opponents* of patent attorneys or do they consider themselves as working for a common objective: the issuance of valid patents?

Finally, Congress and the Federal judiciary represent the other two branches of the U.S. government which deal with patents. When one considers the terrific pressures to which legislators must be subject, the restraint that U.S. legislatures have shown in keeping patent law changes to a minimum through the years seems remarkable. Also, when one considers the complexity and variety of patent cases which the judiciary has had to rule on—and let us not forget the probable fact that only questionable cases are brought to court—one must gaze with awe at the overall record of Federal judges.

However, if the members of the Patents Committees of Congress knew more about the every day working of the minds of inventors and the problems of investors and the other groups, Congress

*Richards and Cifelli, Newark, New Jersey

STRIKING CAN DESIGN AND LITHOGRAPHY GIVE PRODUCTS INSTANT BRAND IDENTIFICATION . . .

Aren't these cans familiar? They are to most people for two good reasons. One, they hold well-known brands. Two, they're packaged for instant recognition in Continental specialty cans. Each can has been made a national landmark by Continental craftsmen. That's because these specialists have an expert way with design and lithography. The colors and patterns they produce are *outstanding*.

Why not put these Continental services to work for you? You're sure to get a can that's just the right size, shape and design to make *your* product a permanent landmark in today's homes.

Continuous message... Continuous design

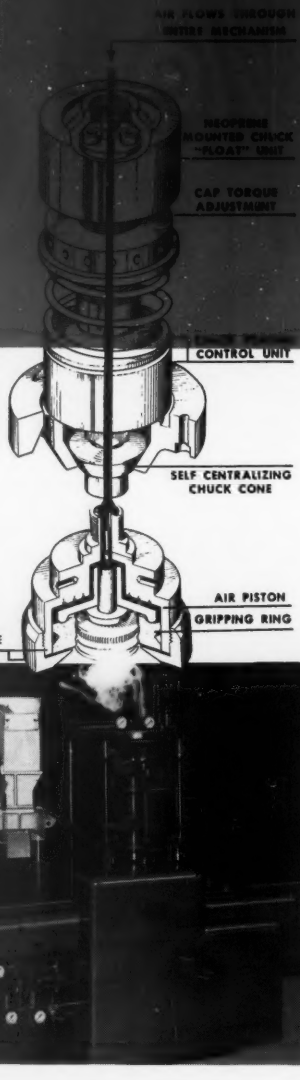
Readily identified in the store, whichever face it shows. Readily identified as a Continental specialty can because of its dramatic lithography. We've a palette-full of colors for your choice.

QUALITY Continental SERVICE

CONTINENTAL CAN COMPANY

Eastern Division: 100 E. 42nd St., New York 17
Central Division: 135 So. La Salle St., Chicago 3
Pacific Division: Russ Building, San Francisco 4

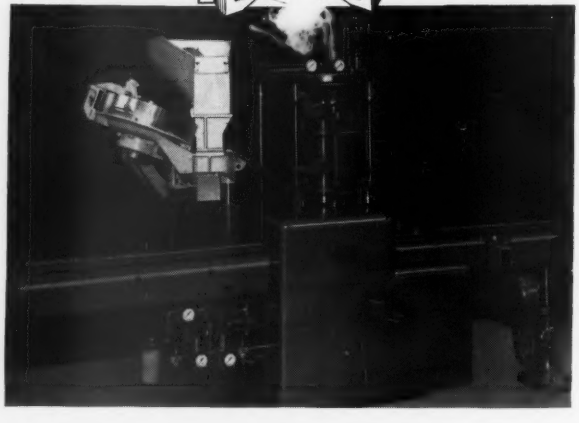
ALL IN A DAY'S WORK for PNEUMACAP



AMAZING ADAPTABILITY COUPLED WITH THE GENTLEST FEED AND TURN-ON ACTION KNOWN

Right from the time the caps are delivered to the hopper of the Sterling Cap Feeder on the PNEUMACAP, to the moment they're turned onto the container, they're handled with kid gloves. There's no churning or grinding in the feeding operation. Caps "dribble" easily into position, on call from the machine. No jamming to cause scratching or breakage.

Then the amazing air chuck takes over. Air pressure firmly squeezes the neoprene doughnut around the cap. Exactly conforming to any turn-on closure – metal, knurled, smooth, molded – it holds the cap in its no-scratch, no-slip grip. Full floating action allows chuck and cap to "find" container top. Choice of four chuck speeds to match caps from partial turn-on lug type to multi-turn long continuous thread closures. Machine is available in two, four, six and eight head models.



PNEUMATIC SCALE CORP., LTD., 70 Newport Ave., Quincy 71, Mass. *Also: New York; Chicago; Dallas; San Francisco; Los Angeles; Seattle; Leeds, England. Canadian Division: Delamere & Williams Company, Ltd., Toronto.*

★ PNEUMATIC

Packaging and Bottling Equipment

might not be as insistent as it has been that the Patent Office should have to pay its own way, a cost which naturally has to be born ultimately by the inventors. Why should inventors, who contribute to the welfare of society, be so considered when Congress is literally handing out billions to other groups? As for the courts, perhaps a better understanding on the part of the judges of the various elements involved in the patent system might result in fewer decisions based on technicalities such as the meaning of particular words, and more decisions based on the broader grounds of equity.

What can or should be done? The answer appears to be simple: education. The real question is how to go about it. Perhaps the most feasible method would be annual symposia for the discussion of patent problems. The timid—and they are legion when it comes to patents—will object that the idea is too radical because it has never been done. Actually, some of the patent law associations and national technical societies have conducted symposia of sorts, regional or national, on occasion. Indeed, far from appearing to be radical, it would seem that symposia meetings on a regular basis, involving all the main groups intersted in patents would really be a step in carrying out the purpose of the patent system: "to promote the progress of science and useful arts," as laid down by a legal document hundreds of years old, the U.S. Constitution.

Mr. Bush's Proposal

In the last two issues of this journal the proposals of Dr. Bush for improving the patent system were published in part. These proposals fell into three categories as follows:

A. Purposes and Objectives of the Patent System
B. Current Problems of the Patent System, and
C. Recommendation for Improving the Patent System
D. Conclusion.

Parts A. and B. have already been published. Dr. Bush's proposals, in his own words continues:

For Improving

There are many aspects to this problem of strengthening the system. The following suggestions are offered, not because they are regarded as in any sense a cure-all, but because they seem to get at the heart of several of the primary difficulties of the system as it stands. Many other suggestions could be offered and have been offered. I am not sure that after full discussion and argument I would still support the legal remedies I present; these suggestions may have serious faults which I do not now see. But I have felt that this statement should attempt, if possible, to get down to brass tacks and not end in generalities. I hope, at least, to provoke discussion of the explicit and the concrete.

1. *Increase the presumptive validity of patents*

(*1*) *The Patent Office should exert more effort to insure that the patents it issues are truly valid*—.To this end, the Congress should make larger direct appropriations to the Patent Office. The additional funds should be expended both for personnel and for facilities. At the present time there is a considerable backlog of work in the Office, and the staff is heavily loaded. For one matter, a reclassification of patents, badly needed to bring the work up to date, cannot be completed for some years. The Commissioner of Patents should have an adequate staff, freed from routine duties, and capable of planning ahead and of studying means for facilitating current work.

(*b*) *More complete Patent Office examination of prior art: improved classification, adequate budget.*—A more careful acquisition and examination of technical literature, both domestic and foreign, by the Patent Office before a patent is issued will distinctly lessen the possibility that issued patents will be overthrown on the basis of previously unnoticed publications. A committee, of which I was chairman, recently recommended that mechanization for the search of literature and prior patents be introduced in the Patent Office, and proposed ways of arriving at this result.[50] Appropriate mechanization is greatly facilitating the conduct of various forms of business. It appears that it could be of especial benefit in the Patent Office. There are some 7 million documents in the Office to which reference is made in the course of examination of an application. Even so this by no means covers the publication which may be pertinent. In spite of a system of classification to aid search, and in spite of the fact that about half the time of 600 examiners is spent in searching this complex maze of material, it is inevitable that important references will be overlooked.[54] Many times, when this occurs, it places a severe burden on industry, the courts, and the inventor himself. An invalid patent can do a lot of damage. There are those who feel that this particular problem, because of its diverse nature, can not be readily solved by mechanical means. Certainly the experience of examiners, who have become familiar with special fields through long experience should not be sacrificed. But modern data-handling equipment is exceedingly flexible and versatile. It is often thought of, by those who do not understand it, as a mere card shuffling affair. But it is far more than this. It can have a memory, so that the experience of one search will become available to other searchers. It can be fast and comprehensive. It can even be arranged to facilitate its own evolution, as its subject matter grows and the art changes. The arrangements for proceeding toward an adequate and well-thought-out mechanization are excellent. There is a committee in the Office studying the applicability.[55] The Bureau of Standards has undertaken to investigate the best applicable mechanism. An advisory committee, of highly competent individuals serving voluntarily, is engaged in guiding the development. I trust that adequate funds will be available for the support of this important move.

There is the strongest kind of public interest in having this job done well. It cannot be accomplished without additional staff and additional funds. Moreover, the necessary additional money should come from public funds and not from inventors' fees. This is a matter of public responsibility. The cost of patent administration cannot be made primarily the responsibility of the inventors through patent fees without unduly burdening many worthy inventors.

It should not be forgotten, in this connection, that the body of issued patents is intended to supply to citizens generally a complete reference on the current state of technical fields in which progress is being made. It has by no means, in recent years, been as valuable in this regard as it might be. This is partly due to its great bulk, and partly due to the difficulty of consulting it in its present form. If it were fully mechanized, and especially if its subject matter included literature references as well as prior patents, it could become very useful indeed. In fact, by making duplicate cards or tapes or the like available, there could be made available to libraries and to inductry a highly valuable means of keeping up to date in our rapidly evolving techniques. There is no way, in my opinion, that the Department of Commerce could be of more genuine aid to industry

(*Continued on page 855*)

WE PREDICTED...
WE PIONEERED...
WE'RE PRODUCING...

Polysols®

the revolutionary approach to pressure packaging that now opens up a new and tremendous market to

ANY PRODUCT THAT FLOWS

Polysols are now in production

Connecticut Chemical opens the door to thousands of manufacturers who are seeking new markets, broader consumer acceptance, and long-range profits. In POLYSOLS lie the pressure packaging future for literally unlimited products *already on the market*—and many more *still to be born.*

POLYSOLS, developed by Connecticut Chemical, are a revolutionary new concept in pressurized packaging which has made it possible to package in "pushbutton" form almost any cosmetic, drug, pharmaceutical or household product *that flows*, or *can be sprayed.*

In the drug field alone the application of POLYSOLS for gargles, depilatories, toothpastes, liniments, lotions, ointments and body rubs are virtually limitless.

Aerosol field was limited in scope

Until now, aerosols have been confined in their applications because refrigerant gases were incompatible with many products, many chemicals, many containers, or unacceptable for internal use.

Examples: refrigerant propellants couldn't be used for baby oils that must be expelled at room temperature... products to be used internally as mouth washes and nasal sprays... highly viscous materials such as toothpastes... or products with water base emulsions, such as furniture polish.

Packaging revolution pioneered by Polysols

The POLYSOL concept, packaged in highly diversified ways, was introduced to industry during a press conference at the Waldorf-Astoria in May 1956. Since then even greater strides have been made in research and development.

Many gases not heretofore used in pressurized packaging including nitrogen, CO_2, nitrous oxide and other rare gases — *were adapted depending upon the individual requirements of each particular product.*

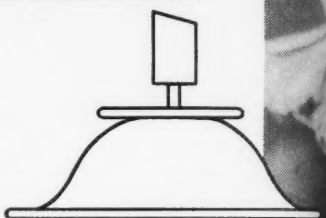
Just as important, our laboratories worked with the assistance of valve and container companies in developing further refinements in the design of valves, siphon tubes, internal coatings and containers. This cumulative technical pioneering was responsible for many great POLYSOL achievements.

Improve your product—or create new ones!

Consumers have long recognized the enormous advantages of pressurized products. Their acceptance has been truly fantastic. And now, Connecticut Chemical makes possible the production of countless, *new* products in pushbutton form... with tremendous sales volume opportunities... costing but slightly more than present packaging methods.

Our research development laboratories are in a position to offer you sound technical advice. We can show you how POLYSOLS can be applied to your product or help you conceive a new one. Above all, we can help you determine if your product should be in POLYSOL or *aerosol* form.

CALL OR WIRE TODAY— and let us show you how POLYSOLS may be the solution to your problems. Even if your product was checked in the past, *and found to be too costly or impractical*, we can prove to you that POLYSOLS can be your economical answer.



QUICK POLYSOL FACTS

Q What are POLYSOLS?

A POLYSOLS are a combination of non-liquefied gases used singly or in combination... plus skilled packaging techniques... all designed to fit individual product requirements.

Q Are POLYSOLS expensive?

A Economy, is the word for POLYSOLS. Many manufacturers are discovering POLYSOLS cost but slightly more than old standard methods.

Q Can POLYSOLS be ingested safely?

A POLYSOL propellants are harmless. They're as safe as the product they propel... safe even for use on infants.

Q How can POLYSOLS boost sales?

A They enable you to offer an easily dispensed product... in an attractive, hermetically-sealed package... with economy. And they give you a new, powerful advertising story!

Polysols open the door to almost any product—for example:

Cosmetics
Cleansing creams
Facial creams
Vitamin creams
Astringent creams
Shampoos
Hair creams
Wave sets, lotions
Dandruff remedies
Hand creams
Cologne creams
Deodorant creams
Sun tan aids
Hair tints
Hair conditioners
Hair dyes
Liquid makeups

Drug Items
Toothpastes
Antiseptics
Body rubs
Hemorrhoid creams
Electric shave lotions
Hair grooms
Hair lotions
Baby astringents
Mouth washes
Liniments
Salves
Burn creams, lotions
After shave lotions
Diaper rash creams
Baby oils
Nasal sprays

Household & Other
Disinfectants
Spot removers
Metal polishes
Shoe polishes
Shoe cleaners
Car waxes
Furniture polishes
Furniture waxes
Detergents
Auto cleaners
White wall tire cleaners

Food—Already 30 food items have been successfully packaged to date—and Connecticut Chemical has made technical assistance available to interested food manufacturers and purveyors.

It's here
A TOOTHPASTE!

It's here
A FURNITURE POLISH!

It's here
A DEPILATORY!

It's here
A WAVE SET!

CONNECTICUT CHEMICAL RESEARCH CORPORATION

BRIDGEPORT 5, CONN.

CANADA: Connecticut Chemicals Canada, Ltd., Curity & Hollinger Rd., Toronto
ENGLAND: Midland Aerosols Limited, Wolverhampton

HOW YOU CAN

PACKAGE FOR PROFIT IN 1957

Growth aerosols point the way to volume sales

Market studies point to huge potential sales for growth aerosols—products which have not yet been widely promoted in aerosol form. Many products, like colognes, personal deodorants, hair lacquers, hair tints, hair dressings and conditioners, and sun-tan lotions, which have large total sales in all forms of packaging, are now available in aerosols.

And, whenever housewives try these products in aerosol form, they show an overwhelming preference for them. Surveys reveal that aerosol features like ease of use, spill-proof package and no loss or waste in storage or use rate high with housewives.

High preference for aerosol packaging, plus a large total market for these products, points to a big-volume potential for aerosol-packaged products. Why not package your product for profit in an aerosol?

"Demonstration SELLS aerosol sun-tan oil," reports a Miami department-store manager. "Once a customer sees how easy and effective aerosols are to use, she's sold. For drug and cosmetic products, aerosols are one of today's most exciting sales stimulators."

Du Pont can supply the right Freon* propellent for your aerosol product

Propellent requirements of your aerosol product for pressure, solubility, stability and particle size are sure to be met by one of the over 25 "Freon" propellent solutions available from Du Pont. "Freon" propellents are nonflammable, nontoxic, noncorrosive and uniformly high in quality. They are backed by more than 26 years of Du Pont's manufacturing leadership and the industry's most comprehensive technical and marketing services. For more information or assistance write to E. I. du Pont de Nemours & Co. (Inc.), Freon® Products Division 1511 Wilmington 98, Delaware.

**Freon and combinations of Freon- or F- with numerals are Du Pont's registered trademarks for its fluorinated hydrocarbon propellents.*

FREON® *propellents*

DU PONT
REG. U. S. PAT. OFF.

BETTER THINGS FOR BETTER LIVING...THROUGH CHEMISTRY

News in Packaging . . .

Tamper-proof Bottle

A tamper-proof flint bottle is being employed by King Research, Inc., Brooklyn, to package its new concentrated Dandricide anti-dandruff rinse. The four-ounce private mold bottle was designed and is being produced by the Hazel-Atlas Glass Division of Continental Can Company.

The bottle's white Alcoa cap, printed with instructions for use of the anti-dandruff product, is held fast by a seal, which, if broken, readily reveals that the bottle has been tampered with. The cap is also used to measure the liquid which is then diluted into an eight-ounce glass of water before application.

New American Can Plant in Ohio

American Can Company formally opened its newest can-making plant at Blue Ash, Ohio, Oct. 31 during dedication ceremonies attended by some 150 Ohio civic, political and business leaders.

Central division vice-president F. B. Newcomb said the new plant accented the company's "concept of service—the broadening and decentralizing of its operations to bring sources of supply to the front door of its customers." The 240,000-square-foot plant has a manufacturing capacity of about 200 million metal containers a year.

RONALD P. O'HANLEY

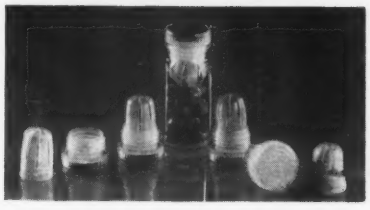
O'Hanley In New Scovill Post

Ronald P. O'Hanley Jr. has been appointed coordinator of advertising and market research for the Cosmetic Container Division of Scovill Manufacturing Company. He will report to William H. Harris, sales manager of the division.

Mr. O'Hanley joined Scovill in 1954 and has been assistant to the advertising manager of the Closure Division.

New Pill Bottle Closure

A new polyethylene pill bottle closure, designed to prevent movement and breakage of tablets while being transported, is being offered for sale or manufacture under license in the United States by Pegasus International Cor-



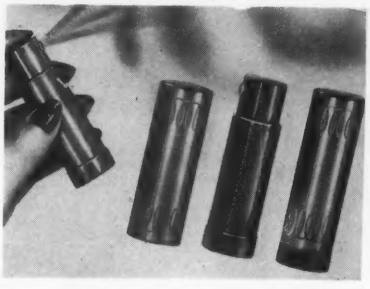
poration, 1 East 53rd Street, New York 22.

An integral part of the container's cap, the closure comes in three basic styles to accommodate various shapes of containers used in the drug industry.

Crown Cork Appoints Beeler

Richard W. Beeler has been appointed manager sales development of the Can Division of Crown Cork & Seal Co., according to Edward P. Stuart, division manager of sales. Mr. Beeler formerly was manager of sales development of the company's Crown and Closure Division.

Richford Corporation has introduced Touch-N-Spray, an aerosol perfume atomizer with a plastic container and a long, gold-metal cap which insures against accidental discharge.



1960 Aerosol Hair Lacquer Sales Of $187,500,000 Predicted

Highest dollar-volume cosmetic item in 1960 will be aerosol hair lacquer, according to Douglas Atlas, vice-president of G. Barr and Company, who predicts that hair lacquer output will increase to 150,000,000 units annually within the next two years.

At an average retail price of $1.25 per unit, hair lacquer will reach an annual volume by 1960 of $187,500,000—more than will be spent for lipstick, face powder, home permanents, or any single toiletry excepting soaps and dentifrices, says Mr. Atlas, who bases his prediction of 150,000,000 units on increasing numbers of women discovering the spray method of hair "manageability," as well as on greater frequency of hair spraying by the individual user. A total of 80,000,000 units was produced in 1956, and 100,000,000 are expected for 1957.

Mr. Atlas said that technical advances resulting in longer "holding power" for the hair, a more natural feel, and "re-combability" after hair lacquer application are helping establish the product as a toiletry "must" among the 65,000,000 women who comprise the American cosmetic-using age group. He said that 70 per cent of this group used an average of 1.7 containers of hair lacquer in 1956 and that "as women grow accustomed to and dependent upon hair lacquer, they will use it consistently rather than occasionally as figures indicate they did last year."

FRED R. GARDNER

Sales Mgr. of Aerosol Techniques

Fred R. Gardner has been appointed sales manager of Aerosol Techniques, Inc., it has been announced by H. R. Shepherd, president. Mr. Gardner was formerly with Stein Hall & Company. From ATI's New York offices, Mr. Gardner will direct the company's expanded sales program among cosmetic, pharmaceutical and food marketers.

Chocolate
Coffee
Tea
Toppings
Batters
Catsup
Syrups

Waxes
Cleaners
Detergents
Hand Lotions
Dental Creams
Hair Dressings
Shampoos
Shaving Soaps

Wonderful way to Package ...for any

NON-AERATED LIQUID STREAM

A STREAM DISPENSER that operates at the touch of a finger. It's non-aerated and it maintains an hermetic seal on the container contents. Normally reactive volatile or oxidizable products can be kept for long periods of time without refrigeration... kept exactly as they were packaged. This makes an ideal container for foods, toiletries and household helps. Ideal because the contents remain unchanged after packaging. Ideal because it is an eye-appealing and easy to use package that has proven sales motivation.

PRECISION VALVE CORPORATION

liquid or semi-liquid product -Precision's new valve and spout

Sweeteners

Flavorings

Ethical Pharmaceuticals

Antibiotics

Liquid Makeups

Prescription Dispensing

Eye Drops

Vitamins

Tabasco

Bitters

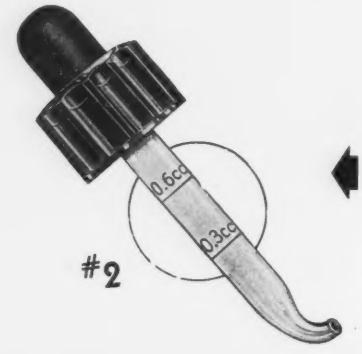
Nose Drops

DROPS MEASURED TO SIZE

A DROP DISPENSER that operates at the touch of a finger to give a predetermined drop size, exact enough to dispense drugs or vitamins. An ideal dispenser of volatile products, many medicinals or oxidizable vitamins and extracts. The inert propellant does not effect the contents either physically or chemically. Thanks to Precision, you can now take advantage of this most modern and effective packaging container. Precision's engineers will be most happy to discuss your product and your product problems . . . a letter will bring you complete details. Why not write today!

700 Nepperhan Avenue, Yonkers, N.Y.

New Perfection DROPPING PARTS

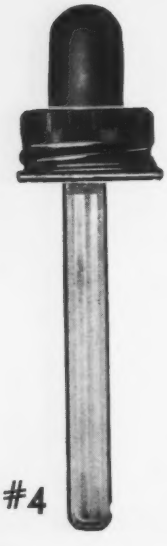


ACCURATELY ◆◆◆ CALIBRATED In Any Color

This Inexpensive EXTRA FEATURE Adds A Welcome Convenience To The Use of Your Product

Accurate calibration of New Perfection dropper glasses adds immeasurably to the user's satisfaction with your product. Not only is the specified dose measured with more precision, but the tedious and time-wasting practice of counting drops is made unnecessary.

Trade-marks or firm names may also be imprinted on the glass, assuring that the name will be identified with the product each time it is used.



We can supply various colors of bulbs in natural rubber or in our special oil-resisting Amokine compound, caps of plastic or metal in many sizes and colors, and various types of dropper glasses in any length. New Perfection dropping parts will fit your own bottles, or can be supplied in combination with our Modernistic bottles in Amber, Blue, Green or Clear glass. Sizes: 1/8, 1/4, 1/2, 1 and 2 oz.

Write for Samples and Quotations

PENNSYLVANIA GLASS PRODUCTS CO. INC.

"Glass Goods of the Better Kind"

430 N. CRAIG ST. • PITTSBURGH 13, PA., U. S. A.

Out of this world beauty for Mr. and Milady

In crystal-clear flint and beautiful opal, Hazel-Atlas *Private Mold* Containers are imagination in glass — and practical, too. At domestic prices, they add the glamorous prestige of more expensive imports to your men's and women's cosmetics. And to save you time and expense, distinctive H-A "Deco-fired" Cosmetic Labels and designs can be economically applied in one or several permanent colors at the time of manufacture.

Rigid quality-controls keep your H-A containers uniform in size, shape, clarity and color. They perform efficiently on the filling line and display your product at its best. You are sure of fast, dependable delivery during sales peaks and emergencies, served by H-A's nationwide network of glass plants and warehouses. A beautiful line of stock containers is also available. Call your nearest H-A representative, today.

...glamour in glass

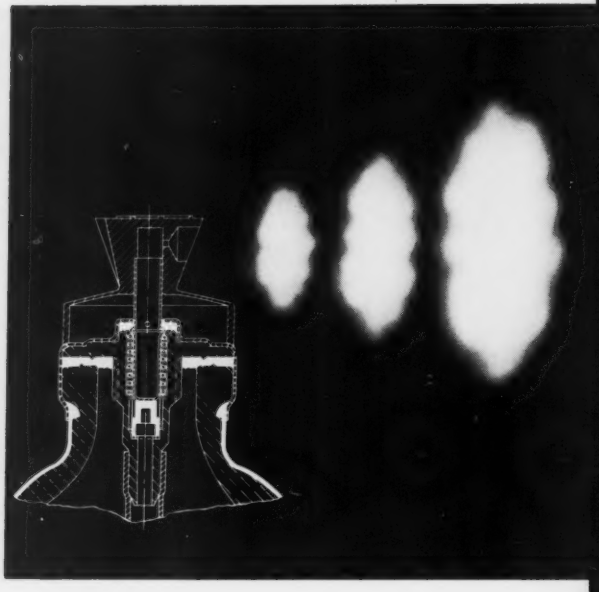
HAZEL-ATLAS GLASS division of CONTINENTAL CAN COMPANY

WHEELING, WEST VIRGINIA

Creating New Horizons
In Cosmetic And
Pharmaceutical Packaging

RISDON METERED SPRAY AEROSOL VALVES

For Coated Glass Containers



For Metal Containers

Creative research has made the Risdon metering valve another facet of Risdon's leadership in aerosol product dispensing.

You will find it in use on exquisite containers dispensing measured amounts of many of the best known perfumes. And in the pharmaceutical field, its ability to deliver the various pre-measured dosages desired, through special applicator-actuators, is opening new aerosol product possibilities.

It is available with either standard or patented Risdon "Micro-Mist" actuators, permitting unprecedented formulation latitude.

To serve your aerosol dispensing requirements Risdon offers technical advice and assistance plus extensive research, testing and quality control facilities and a fund of successful experience in the production of valves for a wide range of products.

For further information on Risdon metered-spray or conventional spray valves for glass, metal or plastic containers, contact Risdon today.

RISDON

THE RISDON MANUFACTURING CO.

Valve Division, Naugatuck, Conn.

For Combination Glass & Metal Containers

Available with Special Applicator-Actuators For Pharmaceutical Products

RI-96

another RICHFORD First:

TOUCH-N-SPRAY

TRADEMARK

THE ALL PURPOSE AEROSOL PERFUME ATOMIZER FOR THE PURSE

TOUCH-N-SPRAY Refillable ...

TOUCH-N-SPRAY Long Gold Metal cap to prevent accidental activation.

TOUCH-N-SPRAY So easy to use—so light in weight—so very, very smart.

Write NOW for samples and prices

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Silky soft... demurely manageable with TRITON X-400

It takes only one glance and a stroke of the comb to tell when hair has been rinsed with cream formulations containing TRITON X-400. By removing soap film and providing necessary lubrication without grease, this cationic quaternary ammonium compound makes hair silky soft and pleasingly lustrous. At the same time, TRITON X-400 reduces static electricity to make hair more manageable and easier to comb. Put TRITON X-400 to the test. See your Rohm & Haas representative or write direct for samples.

Chemicals for Industry

ROHM & HAAS COMPANY

WASHINGTON SQUARE, PHILADELPHIA 5, PA.

Representatives in principal foreign countries

TRITON *is a trade-mark, Reg. U.S. Pat. Off. and in principal foreign countries.*

NEWS...

New Mead Johnson Dept.

Dr. Donald L. Timma has been appointed to direct Mead Johnson & Company's new scientific methods and instrumentation department. The newly established department is concerned with developing and implementing methods and techniques of conducting scientific analyses through use of new mechanical, optical and electronic instruments, the analyses to be used for the development of new pharmaceutical preparations and in product quality control.

Bowman Is B-M Director

Election of Dr. Philip I. Bowman as a director of Bristol-Myers Company has been announced by Henry P. Bristol, chairman of the board.

Dr. Bowman joined Bristol Laboratories in 1944 as production manager, became plant manager in 1945 and a vice-president in 1946. In 1947, he was named a director of Bristol Laboratories and in 1949, an executive vice-president.

Research Dir. of van A-H

Dr. Ernst T. Theimer has been appointed director of research for van American-Haebler, Inc., according to an announcement by Charles P. Walker, president. Engaged in various research activities with the firm since 1931, Dr. Theimer's new responsibilities include direction of research on aromatic products and processes as well as on new analytical techniques for product quality control.

DR. ERNST T. THEIMER

Warner-Chilcott Res. Dir.

Dr. Charles C. Scott has been appointed director of research for Warner-Chilcott Laboratories, according to Dr. Leonard A. Scheele, president. Dr. Scott succeeds Dr. George Mangun who has become a research consultant.

For seven years Dr. Scott has headed Warner-Chilcott's department of pharmacology. Previously, he was head of the department of general pharmacology at the Eli Lilly Company.

SCC Election

President-elect of the Society of Cosmetic Chemists is Savery F. Coneybear, according to an announcement. Robert A. Kramer has been elected secretary; Walter A. Taylor, treasurer; and Sophie L. Plechner and Paul G. I. Lauffer, directors.

Ballots cast totaled 344, compared with 287 last year. But only 126 nominating ballots were received before this year's election.

SYDNEY A. FINER

Sydney A. Finer to Retire

Sydney A. Finer, head of the Clinton, Conn., plant of Chesebrough-Pond's Inc., will retire January 1, 1958, it has been announced by Jerome A. Straka, president, who said that "the entire Chesebrough-Pond's organization will miss Mr. Finer's fund of knowledge in cosmetics manufacture, as well as his administrative ability. We wish him many happy years."

Mr. Finer, who started with Pond's Extract Company in 1916 as a shipping clerk, became vice-president in 1944, and vice president of the Pond's Extract Division of Chesebrough-Pond's Inc., when the two companies merged in 1955.

Born in Croydon, England in 1892, Mr. Finer has lived and worked in Clinton ever since he came to this country in 1911. He and his wife, Pauline, intend to keep up their home in Clinton with occasional trips to "follow the sun."

ANDREW A. LYNN

Andrew Lynn Accepts Post With Chesebrough-Pond's

Andrew A. Lynn has been appointed to the newly created position of vice-president of domestic marketing for Chesebrough-Pond's Inc. and to the company's board of directors, according to an announcement by Jerome A. Straka, Chesebrough-Pond's president. Prior to his appointment, Mr. Lynn had been vice-president in charge of sales for Revlon, Inc.

Mr. Straka also announced the retirement of Edward D. Lane as vice-president in charge of domestic sales and as a director. Mr. Lane will continue his association with the company as a consultant.

In his new post, Mr. Lynn will have full responsibility over all the domestic marketing functions, including sales, advertising, merchandising, sales promotion, and market research.

He started his career in Poland as a Colgate-Palmolive salesman in 1930 and rose to acting general manager in that country before World War II curtailed Colgate's operations there. Arriving in the United States in 1940, he started again and became a general sales supervisor for Colgate in 1942 and merchandising manager of the Toilet Soaps Division in 1944. By 1946 he had become a citizen of the United States, and he was named general merchandising promotion manager of the Soap Division in 1952. He joined Revlon as vice-president in charge of retail sales in 1954, and became vice-president in charge of domestic sales two years later.

Mr. Lane started as a Pond's Extract Company salesman in Atlanta in 1933. He was promoted to sales manager for Pond's in 1947, and named vice-president in charge of sales in 1949. At the time of the Chesebrough-Pond's merger he became vice-president in charge of domestic sales, and a member of the board of directors.

THE NOSE

Fancy and Fact

Fancy

According to Greek Mythology, Prometheus fashioned an image of a man out of clay, then snatched fire from the sun and held it to the nostrils of his clay figure. The figure sneezed and came alive.

Fact

PFW's great line of balanced perfume bases and specialties can make your products come alive with fragrances of great beauty and tenacity.

PFW

for odor and taste

POLAK'S FRUTAL WORKS INC., MIDDLETOWN, N. Y.

AMERSFOORT, HOLLAND • PARIS, FRANCE • BREMEN, GERMANY • BRUSSELS, BELGIUM • SOFLOR LTD. - PERIVALE, ENGLAND

Lilly Promotes 3 Scientists

In recognition of their research contributions, three scientists have been promoted by Eli Lilly and Company. Jack Mills, Ph.D., has been appointed a research advisor; Richard S. Griffith, M.D., senior physician; and Robert L. Mann, Ph.D., research associate.

Dr. Mills has made contributions in the fields of antihistamines, hypnotics, ulcer therapy, and drugs to treat Parkinson's disease. During the last three years he has helped synthesize and study new drugs for mental illness. In 1952 he received recognition for earlier research accomplishments with Lilly by being promoted to the post of research associate.

Dr. Griffith has been associated with the Lilly Laboratory for Clinical Research at Indianapolis General Hospital since 1946. He did his first Lilly research work in the field of cardiovascular disease, but since 1953 he has been responsible for research in infectious diseases.

Dr. Mann has made major contributions to research on hygromycin, a new antibiotic, and hygromycin B, a new antibiotic with anthelmintic properties. He was responsible for hygromycin's isolation and characterization and the elucidation of its structure. He also contributed to research on erythromycin and studied its metabolism.

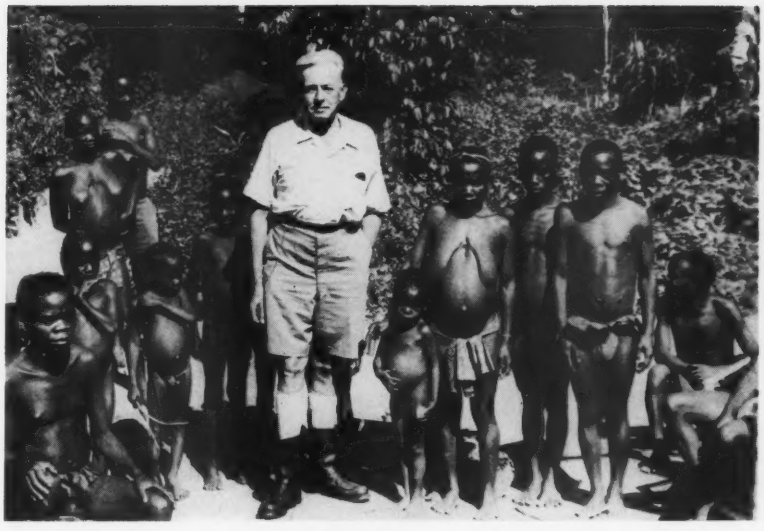
Will & Baumer Names Lannon

Robert E. Lannon has been appointed sales manager of the fancy candle division for Will & Baumer Candle Company, it has been announced by Leonard P. Markert, vice-president and general sales manager. Mr. Lannon succeeds Leo Nerenberg, who has retired after 54 years with the firm.

Shulton's Chicago Asst. Mgr.

Donald L. Averill has been named assistant manager of the Chicago sales office of Shulton, Inc.

DONALD B. BLACK



Among the pygmies of the Ituri Forest, Belgian Congo, is Dr. Ernest Guenther, vice-president and technical director of Fritzsche Brothers, Inc., during his recently completed six-month safari through Africa to study essential oil production. Dr. Guenther, who wrote on-the-spot reports while in Kenya Colony, southern Africa, Madagascar, the Comoros and Reunion Island, is now back at his New York office. Fritzsche plans to continue distributing these reports to the industry, datelined at the time and place written, until Dr. Guenther's full account of his experiences and findings is completed.

MS&D Int. Vice Presidents

Huskel Ekaireb, Leo Fernandez, and Alfred D. Freund have been elected vice-presidents of Merck Sharp & Dohme International, with responsibilities for specific major areas of the firm's overseas operations, it has been announced by Dr. Antonie T. Knoppers, president of International.

Dr. Knoppers said that these elections reflect the increasing importance of the company's expanding business abroad.

Mackenzie, Mazza Promoted

Frederick Mackenzie, plant engineer of Shulton, Inc., has been promoted to chief engineer, succeeding Nicholas Fowler who has resigned, it has been announced by Victor E. Sommer, plant manager. Eugene Mazza, head of the processing department, has been promoted to plant engineer.

GEORGE E. HARDY

O. Wayne Davis Retiring

O. Wayne Davis of Kansas City, professional representative of the Bristol-Myers Products Division, who is retiring after 30 years with the company, was honored Nov. 20 at a dinner in Kansas City's Muehlebach Hotel. He will reside at Blue Springs, Mo., where he has a 40-acre farm.

Present at the dinner besides Mr. and Mrs. Davis were G. S. McMillan, vice-president of Bristol-Myers Products Division; F. H. Fletcher, assistant vice-president; and N. B. Bullard, manager of the professional representatives department, all of whom flew from New York.

Pharmaceutical Chemicals Section Is Formed by Dow

Organization of a pharmaceutical chemicals section with responsibility for stepping up service to the pharmaceutical industry has been announced by The Dow Chemical Company.

The new section takes the place of the former fine chemicals section, and George E. Hardy has been appointed product manager. Mr. Hardy, formerly on the fine chemicals staff, will coordinate sales activities for the company's pharmaceutical chemicals line.

Donald B. Black, who has been in charge of the fine chemicals section for several years, has been transferred to the staff of Leo B. Grant, sales manager of the chemicals department, and will handle special projects.

Make SHELL your headquarters

Methyl isobutyl ketone is a medium-boiling, active solvent for a wide range of materials used by industry.

In surface coatings of the nitrocellulose and vinyl types, MIBK has excellent solvent characteristics and good tolerance for many hydrocarbon diluents. These same characteristics recommend MIBK for use in lacquer thinners.

As a selective solvent, MIBK is used as an extractant in the manufacture of antibiotics and in the de-oiling of paraffin wax. It finds use, too, as a solvent for synthetic rubber cements and other adhesives.

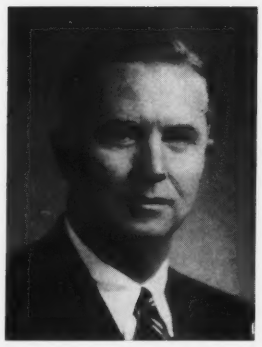
MIBK is also used in the manufacture of such products as fungicides, textile coatings, leather finishing, pharmaceuticals, germicides and the denaturing of ethyl alcohol.

Your Shell Chemical representative will gladly discuss your specific solvent needs with you. For your files, write for: *Organic Chemicals*, a catalog of Shell Chemical solvents, resins and intermediates.

SHELL CHEMICAL CORPORATION
CHEMICAL SALES DIVISION 380 Madison Avenue, New York 17, New York

Atlanta • Boston • Chicago • Cleveland • Detroit • Houston • Los Angeles • Newark • New York • San Francisco • St. Louis
IN CANADA: Chemical Division, Shell Oil Company of Canada, Limited • Montreal • Toronto • Vancouver

SHELL



DR. J. R. BROWN JR.

Colgate-Palmolive Elects

Dr. John R. Brown Jr. has been elected a director and vice-president in charge of research and development of Colgate-Palmolive Company, according to Edward H. Little, chairman of the board and president.

Dr. Brown was formerly vice-president—research and development of the Spencer Chemical Company.

Givaudan to Move Offices

The Givaudan Corporation and its associate companies, Givaudan-Delawanna, Inc., Givaudan Flavors, Inc. and Sindar Corporation, are preparing new, enlarged executive and sales offices for occupancy in Spring 1958, E. R. Durrer, president, has announced. The company has concluded a long-term agreement, leasing the 7th and a portion of the 8th floors in the Warner Brothers Building, 321 West 44th Street, New York 36. A sizable increase in space will be available at the new location allowing for larger perfume, cosmetic and flavor laboratories.

The 1957 Kimble Methodology Research Award is presented to Dr. John E. Blair, second from right, bacteriologist at the Hospital for Joint Diseases, New York City, by Dr. Paul Kabler, awards chairman of the Conference of State and Provincial Public Health Laboratory Directors, during that organization's recent meeting in Chicago. Watching the presentation are Dr. J. V. Irons, left, chairman of the Conference, and E. J. Rhein, founder of the award and sales manager of the scientific division of the Kimble Glass Company, donor of the honor.

Appoint Gater Vice-Pres.

E. T. Gater has been appointed vice-president in charge of sales and advertising for Sterling Drug Mfg., Ltd., it has been announced by Frederick A. Tilston, president.

A native of Canada, Mr. Gater has been vice-president in charge of advertising and director of Sterling's drug store merchandising program since 1952. He joined the company's advertising department in 1942 and was named manager of the department in 1946. During the past eleven years he has been responsible for the advertising and merchandising programs for all Sterling proprietary and toiletry products in Canada.

Grant, Gaudry Promoted

Dr. Gordon A. Grant, director of research for Ayerst Laboratories since 1946, has been elected a vice-president of the company. Dr. Roger Gaudry, assistant director of research, has been appointed director to succeed Dr. Grant, according to an announcement by W. Boyd O'Connor, president of Ayerst.

Dr. Grant will now devote himself exclusively to over-all research policy and the study of current therapeutic trends in medicine. He will counsel management on the selection of new pharmaceutical compounds and areas in which research may best be directed.

Polak & Schwarz Sr. V. P.

Benjamin d'Ancona has been appointed senior vice-president of Polak & Schwarz Inc. With the Polak & Schwarz organization for 38 years, he held positions with P & S branches in different parts of the world before joining the U.S. company in 1940.

Dani Steinfels, center, general manager and overseer of Kolmar Laboratories' French, English and German plants, meets with four Kolmar executives. Clockwise around table: Dr. A. Wahl, technical manager, Kolmar-Europe; Peter Hoenig, technical assistant to general manager, Kolmar-Europe; Dr. H. Stoffel, manager, Kolmar Cosmetics (Deutschland); and K. Strebel, manager, Kolmar Cosmetics (England) Ltd.

BENJAMIN d'ANCONA

Chatting at the Givaudan cocktail party, held last month at the University Club in New York City, are, left to right: Leon Givaudan of Cia. Brasileira Givaudan; Andre Givaudan of L. Givaudan & Cie., Geneva; J. Myer, Hoffmann-La Roche, Inc.; E. R. Durrer, president of Givaudan-Delawanna, Inc.; Frazer V. Sinclair of Drug & Cosmetic Industry; and Peter Isaza of Cheesebrough-Pond's.

Adolph Potdevin Still Active In Machinery Design at 90

Chairman of the board of Potdevin Machine Company, the firm he founded in 1893, Adolph Potdevin, who is still active in the design of packaging machinery, celebrated his 90th birthday Nov. 15 at a party attended by members of his family and employees of the Potdevin Machine Company.

Responsible for the company's basic engineering and design, Mr. Potdevin holds about 150 patents, first of which he obtained in 1901 for a motorcycle he designed.

Shulton Names Ziegler

Roy Ziegler has been placed in charge of production at both the Newark and Clifton plants of the Fine Chemicals Division of Shulton, Inc., William O'Brien, vice-president and division manager, has announced. Mr. Ziegler had been production manager at the Newark plant.

Stokes Mgr. of Manufacturing

Walter W. Goehring has been appointed manager of the manufacturing department of F. J. Stokes Corporation, according to an announcement by F. J. Stokes Jr., vice-president, operations.

Fourman Lectures at College

Dr. Victor G. Fourman, president of Syntomatic Corporation, is among the guest speakers who have lectured or conducted seminars at the City College of New York for graduate students in food engineering, fundamentals of food technology, and confectionery technology.

Catalin Has Cross Licensing Agreement with French Firm

A cross licensing agreement between Catalin Corporation of America and Societe Francaise D'Organo-Synthese, one of several large technical and commercial chemical firms comprising the Roger Bellon Enterprises of Neuilly-Paris, France, has been completed, Harry Krehbiel, Catalin's president, has announced.

The agreement calls for an exchange between Catalin and the Organo-Synthese of know how, technical information and formulas for chemical intermediates.

College Honors Noble

J. Milton Noble, vice-president and treasurer of the Noxzema Chemical Company, has been awarded a citation by the Washington College Alumni Association for his business achievements.

Bush Joins Fritzsche

Donald H. Bush has joined the Perfume Division of Fritzsche Brothers, Inc.

DONALD H. BUSH

Carbide Forms New Div. Announces Executive Moves

D. B. Benedict has been elected a vice-president of Union Carbide Corporation it has been announced by Morse G. Dial, president. Mr. Benedict has been president of Union Carbide Chemicals Company, division of the corporation. In his new position he will be responsible for the corporation's chemicals and plastics activities.

Mr. Dial also announced the appointment of E. E. Fogle as president of Union Carbide Chemicals Company and H. D. Kinsey as president of the newly formed Union Carbide Olefins Company, also a division of the corporation. The Olefins Company will handle the production and sale of ethylene, propylene, butadiene, and other hydrocarbon products.

Shulton Asst. Perfumer

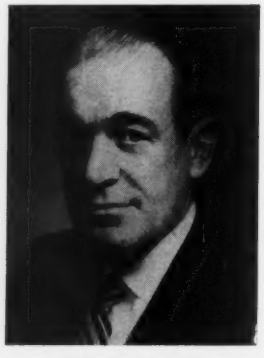
Dorothy A. Douglass has been appointed assistant perfumer in the perfume department of Shulton, Inc., Dr. C. H. Kline, scientific director, has announced. Prior to joining Shulton, Mrs. Douglass had been with the Glidden Company for six years and previously had worked with the technical director of Heyden-Newport Chemical Corporation.

Joins Mead Johnson

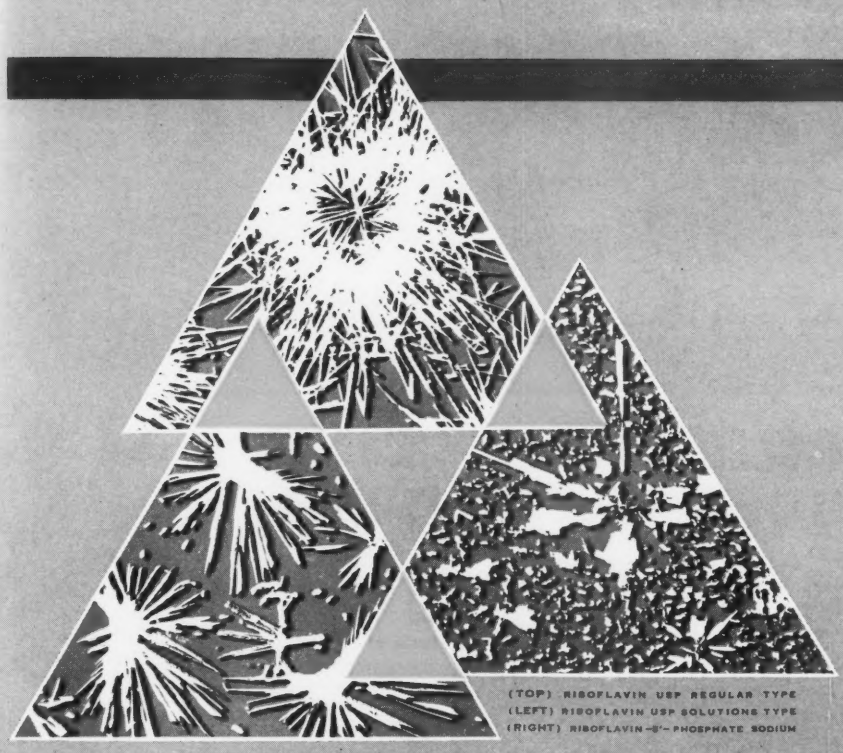
Dr. George W. Brown has been appointed assistant director of clinical research of Mead Johnson & Company. Dr. Brown, a pediatrician, joined Mead Johnson after engaging in private practice in Mesa, Ariz., nearly two years.

Rubinstein Sales Mgr.

Geoffrey B. Smith has been appointed sales manager of Helena Rubinstein, Inc., for both the United States and Canada, according to Oscar Kolin, vice-president.



GEOFFREY B. SMITH



(TOP) RIBOFLAVIN USP REGULAR TYPE
(LEFT) RIBOFLAVIN USP SOLUTIONS TYPE
(RIGHT) RIBOFLAVIN-5'-PHOSPHATE SODIUM

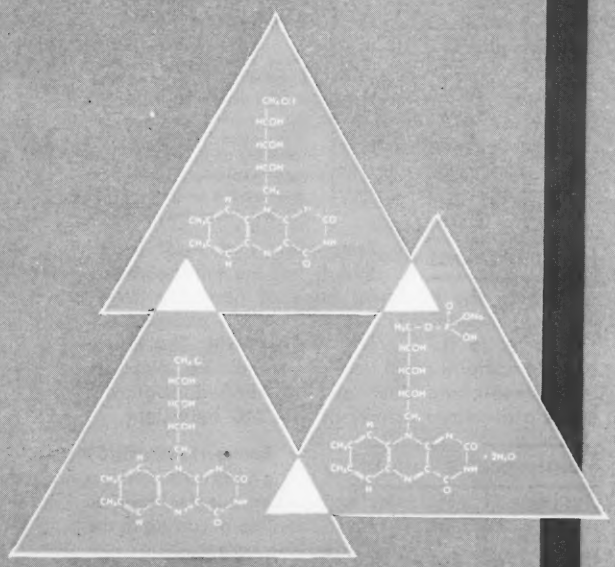
VITAMIN B_2 COMES RIGHT FROM ROCHE

Various types are available to meet the most exacting demands in the pharmaceutical field for tablets, capsules, dietary supplements, liquid preparations; and in the food industry for enrichment premixes and breakfast cereals. Roche has the type of riboflavin that is right for you, whenever you want it—"by the tons."

Roche originated riboflavin-5'-phosphate sodium for all solutions demanding rapid, high solubility, and stability. Among pharmaceutical manufacturers it is preferred for injectable solutions, elixirs, and multivitamin drops. A better, less bitter taste than U.S.P. riboflavin makes it advantageous for chewable tablets and other products likely to be held in the mouth. In the food field it is preferred for breakfast cereals.

The Roche synthesis achieves quality standards that meet, or even exceed the rigid U.S.P. riboflavin requirements. This assurance is insurance for you.

Trust Roche resources for a constant, unlimited supply of riboflavin. Trust Roche for quick, sure service.



ORDER *right* . . . ORDER *from Roche*

VITAMIN DIVISION
HOFFMANN-LA ROCHE INC.

NUTLEY 10, NEW JERSEY, NUTLEY 2-5000 • IN NEW YORK: OXFORD 5-1400

(Illustration represents actual crystals under high magnification, using shadow technique.)

Important Riboflavin Development

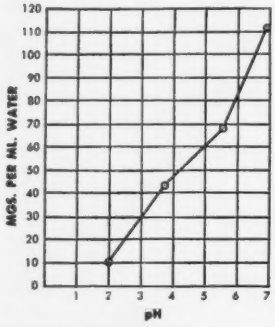
✓ Higher solubility ✓ Better taste

✓ No solubilizer needed ✓ Commercial production

USE ROCHE RIBOFLAVIN 5′-PHOSPHATE SODIUM

higher solubility

Now you can make clear solutions with a concentration of 30 mg. or higher per ml. of water when you use the new Roche riboflavin-5′-phosphate sodium. No longer do you need to use solubilizers and special techniques to achieve a satisfactory solution. Remember the trouble you had in getting a solution of even 2 mg. of riboflavin per ml.? Those days are now past.



SOLUBILITY of Roche riboflavin-5′-phosphate sodium in water at different pH levels; room temperature.

These data show that solubility of Roche B_2 phosphate sodium depends on hydrogen ion concentration in water. It is useful to note that the solubility of riboflavin U.S.P. (approximately 0.12 mg. per ml.) inserted on graph would fall just above the base line.

specifications

Tests show that B_2-5′ (M.W. 514.4) has the full theoretical activity on the molecular basis of riboflavin (M.W. 376.36). Theoretically one gram of the phosphate is equivalent to 0.73 grams of riboflavin. The Roche product contains small amounts of moisture, disodium salt, diphosphate ester and unesterified riboflavin. It has a riboflavin activity of 70-73% by weight.

biological availability

Roche riboflavin-5′-phosphate sodium has immediate biological activity because it is identical with the natural flavin mononucleotide occurring in the "yellow" respiratory tissue enzyme system.

better taste

Roche riboflavin-5′-phosphate sodium does not have the intensely bitter taste of riboflavin itself. It is more palatable in high concentrations. The different taste is of definite advantage in oral preparations.

solubility—taste demonstration

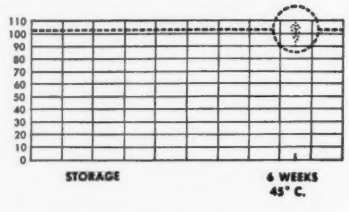
You can prove to yourself, easily and quickly, the solubility-taste advantages of Roche riboflavin-5′-phosphate sodium with the Roche demonstration kit. Ask your Roche representative to show it to you. Or we'll be glad to send one, without charge, at your request.

cost comparison

Even though the cost of Roche B_2-5′ is somewhat higher than regular riboflavin, its use can result in actual savings. You eliminate expensive solubilizers and unnecessarily large amounts of niacinamide. You reduce or eliminate costly complaints and returns. You are able to make manufacturing economies.

stability

Chart demonstrates stability of Roche product in B-complex parenteral solutions with and without vitamin C over wide potency range.



uses

The new riboflavin-5′-phosphate sodium, probably the most important riboflavin development since Roche introduced the vitamin commercially in 1941, is specially designed for use in manufacturing:

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ARTHUR C. GOGARTY

Gogarty Is Tombarel V.P.

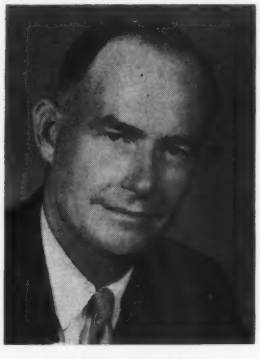
Arthur C. Gogarty has been appointed vice-president in charge of sales and management for Tombarel Products Corporation, according to an announcement by Francois Goby, president of Tombarel Freres S.A., Grasse, France, and Dr. Paul Mulenthaler, president of Tombarel Products.

Mr. Goby, in the United States to visit friends and clients, was present at a celebration held for three employees who have been with the company for twenty years: Howard Miller, vice-president in charge of manufacturing and production; Miss Ann Gilardi; and Mrs. Robert Townes.

U.S.I. Names F. J. Rich

Frederick J. Rich has been named alcohol production manager of U. S. Industrial Chemicals Co., Division of National Distillers and Chemical Corporation, according to Robert H. Cornwell, vice-president in charge of production for U. S. I.

Mr. Rich has been with U. S. I. since 1925. He was plant manager at the U. S. I. alcohol and resin plant at Newark from 1944 until the plant was sold in 1954 and has also been in charge of the company's denaturing and grain alcohol plants at Peoria, Ill., and the denaturing plant at Tuscola, Ill.



CHARLES H. SLATER

Merck Quarter Century Club Rahway Unit Holds Meeting

Two hundred and forty members of the Rahway Chapter of the Merck Quarter Century Club attended the organization's nineteenth annual dinner meeting Nov. 7 at the Elizabeth Carteret Hotel, Elizabeth, N. J. Founded in 1939 with a membership of 127, the club now numbers 406. Other chapters are located in Philadelphia, St. Louis, and Montreal.

Harry B. Colvin was elected president, succeeding George W. Muller. Albert A. Spiro was named vice-president, and Andrew Fabian was re-elected secretary-treasurer. Elected to the executive committee for 1958 were William F. Shields, chairman; Barbara Branney, Philip Gottfried, Edward F. Mooney, Michael W. McCoy, and John N. Bacek.

The following new members inducted earlier this year were introduced: Gabriel Artimovich, Joseph V. Cassio, Joseph Chaiken, Walter Clos, Jr., Frank L. Cohen, Michael Kniazuk, John Lufbery, Hans Molitor, Marjorie F. Smith, Samuel Stein, Andrew E. Strakele, Minnie F. Verillo, Stanley Voorhees, and Andrew N. Wilson.

Principal speakers were the club's honorary president George W. Merck, chairman of the board of directors of Merck & Co., Inc.; John T. Connor, the company's president, and Henry W. Johnstone, senior vice-president of Merck.

Andre Givaudan Visits U.S.

Andre Givaudan ended his semi-annual visit to the United States Nov. 16 when he left on his return trip to Paris and Geneva. While in the United States he visited friends in the industry.

J. T. Baker Promotes Two

Charles H. Slater, assistant to the vice-president in charge of sales of the J. T. Baker Chemical Co., has been promoted to marketing manager, and Warren F. Schumacher, manager of the Fine and Industrial Chemical Division, has been promoted to general sales manager, according to an announcement by Ralph A. Clark, the company's vice-president in charge of sales.

With Baker 23 years, Mr. Slater started as salesman, becoming manager of the New York office, and later divisional sales manager. Mr. Schumacher has also been with Baker 23 years, starting as salesman, becoming manager of the New York Office, and then divisional sales manager. Both executives, in their new positions, will operate from Phillipsburg, N. J.

ROBERT C. DE LOLLIS

Emery Mid-Atlantic Rep

Robert C. De Lollis has been appointed sales representative for the Mid-Atlantic sales territory of Emery Industries, Inc., G. W. Boyd, sales manager of Emery's Fatty Acid Sales Department, has announced.

Mr. De Lollis will handle Emery's complete line of fatty acids, including stearic acid, oleic acid, animal and vegetable fatty acids, hydrogenated fatty acids and glycerides, and caster oil derivatives. He succeeds P. N. Leech, who recently was transferred to Emery's Chicago office.

Honor Weseman at Luncheon

Hans P. Wesemann, vice-president in charge of sales of Fritzsche Brothers, Inc., was honored Nov. 22 at a luncheon celebrating his 40th anniversary with the firm.

The informal celebration at Charles' Restaurant was headed by Fritzsche President John L. Cassullo. Others attending were Fred H. Leonhardt Jr., Dr. Ernest Guenther, E. E. Langenau, Gustave A. Wohlfort, Arthur Hemminger, Ellis Merkl, Val A. Fischer and Jules Bauer.

Joining the Fritzsche organization in 1917, Mr. Wesemann later became director of purchases. In 1941 he was elected vice-president.

WARREN F. SCHUMACHER

AUDREY LANGDON

Audrey Langdon PR Agency

A public relations and public opinion research agency has been started by Audrey Langdon at 6 East 39th Street, New York 16. She was formerly in charge of the public relations activities of the research and development department of Colgate-Palmolive Company. Miss Langdon served as press representative for the Society of Cosmetic Chemists during its recent conference tour in Europe.

Katz Is Ketchum V.P.

Emanuel Katz, former president of Doeskin, Inc., has been appointed to the newly created post of vice-president, marketing, for Ketchum & Co., Inc., Harold M. Altshul, president of Ketchum, has announced.

Charles U. Fisher

Charles U. Fisher, 62, manager of the Parke-Davis Kansas City sales branch, died Nov. 12. A native of Detroit and a graduate of the University of Michigan, Mr. Fisher joined Parke-Davis in 1919, after serving in World War I. He is survived by his widow, Mrs. Jean Fisher.

Walter S. Gay

Walter S. Gay, 55, veteran sales representative of the Glass and Closure Division of the Armstrong Cork Company died Nov. 10 after a short illness. With the company's Chicago district office where he had spent most of his sales career since joining the company in 1921, he had represented Armstrong primarily in the toiletry and cosmetics fields. Among his survivors is his widow, Mrs. Walter S. Gay of Berwyn, Ill.

George W. Simon

George W. Simon, former vice-president of Heyden Chemical Corporation, died November 23, at his home in Bernardsville, N. J. Mr. Simon, who was 85 years old, was born in Germany and was educated in Germany and England. He incorporated the Heyden Chemical Works as a subsidiary of the German house of Von Heyden in 1900.

Retiring from Heyden on April 1, 1944 after many years as director of the company's sales policies, Mr. Simon entered the chemical export business.

During his years with Heyden, Mr. Simon was very active in industry affairs. He was a member of the board of trustees of Columbia University College of Pharmacy; a director of the Synthetic Organic Chemical Manufacturers Association, and a committee chairman of the American Drug Manufacturers Association.

Mr. Simon is survived by his widow, Helen Kny, a daughter, Helen L., and a son, George R.

George W. Merck

George W. Merck, chairman of the board of directors of Merck & Co., died suddenly of a cerebral hemorrhage Nov. 9 at his home, Eagleridge Farm, West Orange, N. J. He was 63.

After graduating from Harvard University in 1915, Mr. Merck joined Merck & Co., which had been started by his father, George Merck. He succeeded his father as president in 1925 when the latter's health failed, serving in that capacity until May, 1950. He became chairman of the board in 1949.

Mr. Merck became a member of the Chemical Advisory Committee of the Munitions Board in 1939 and served as chairman from 1949 until the Spring of 1951, when the committee was dissolved.

He was appointed director of War Research Service when that agency was established in 1942 to take charge of all aspects of biological warfare research and development. In 1944 the War Department assumed full responsibility in this field, and the United States Biological Warfare Committee was established with Mr. Merck as chairman. At the same time, he was appointed special consultant on biological warfare to the Secretary of War. At the peak, 3900 Army, Navy, and civilian personnel were employed in the program.

During World War II Mr. Merck was a member of the Committee on Drugs and Medical Supplies of the National Research Council. In September, 1951, he was appointed by President Truman to succeed Edward L. Moreland on the Board of the National Science Foundation for a term expiring May 10, 1954,

GEORGE W. MERCK

and was reappointed by President Eisenhower for an additional six-year term.

In 1946 Mr. Merck received the Medal for Merit for exceptionally meritorious conduct in the performance of outstanding services to the United States. In 1947 he received the Chemical Industry Medal of the American Section of the Society of Chemical Industry for executive competence in guiding the activities of Merck & Co., Inc., for wartime work for the American Chemical Industry and, in particular, for the human services rendered under his direction. In 1953 he received the award of the Society of Industrial Realtors—"Industrialist of the Year 1953."

He is survived by his wife, Mrs. Serena Stevens Merck, of the West Orange address; a son, John H. C., Amenia, N. Y.; two daughters, Mrs. Francis W. Hatch, Jr., Beverly Farms, Mass.; and Mrs. Frederick Buechner, New York City; two sons by a previous marriage, George Wall Merck, Far Hills, N. J.; and Albert Wall Merck, Mendham, N. J.; three sisters, Mrs. George W. Perkins, New York City; Mrs. Henry Wheeler, Bedford, N. H.; and Mrs. Merck Sheldon, Amagansetts, Long Islang, N. Y.; and nine grandchildren.

Dr. Karl W. von Massow

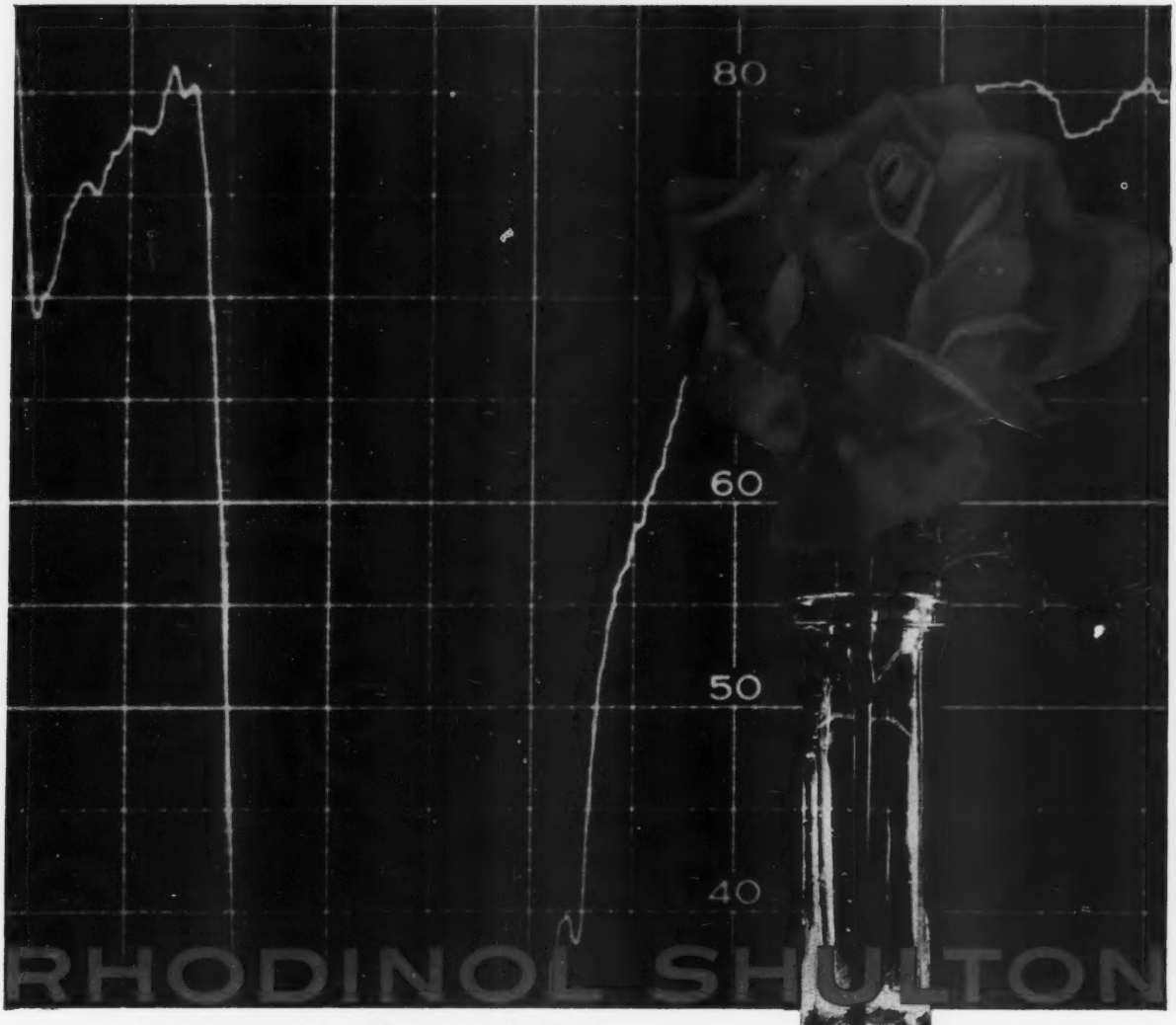
Dr. Karl W. von Massow, chief chemist of the C. E. Ising Corporation for the past fourteen years, died Nov. 16 at Queens General Hospital, Jamaica, N. Y.

Roy L. Zeno

Roy L. Zeno, manager of the water soluble gum department of S. B. Penick & Company for 25 years, died at his home in Hollis, L. I. Nov. 9. He was 63 years old.

Mr. Zeno was a member of The Railroad-Machinery Club of New York and was a former secretary of the Water Soluble Gum Association of the U.S.A.

He is survived by his wife, Carolyn, three sons and three grandchildren.



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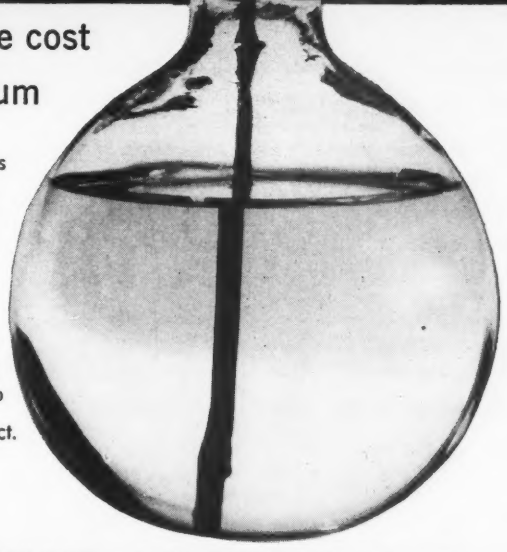

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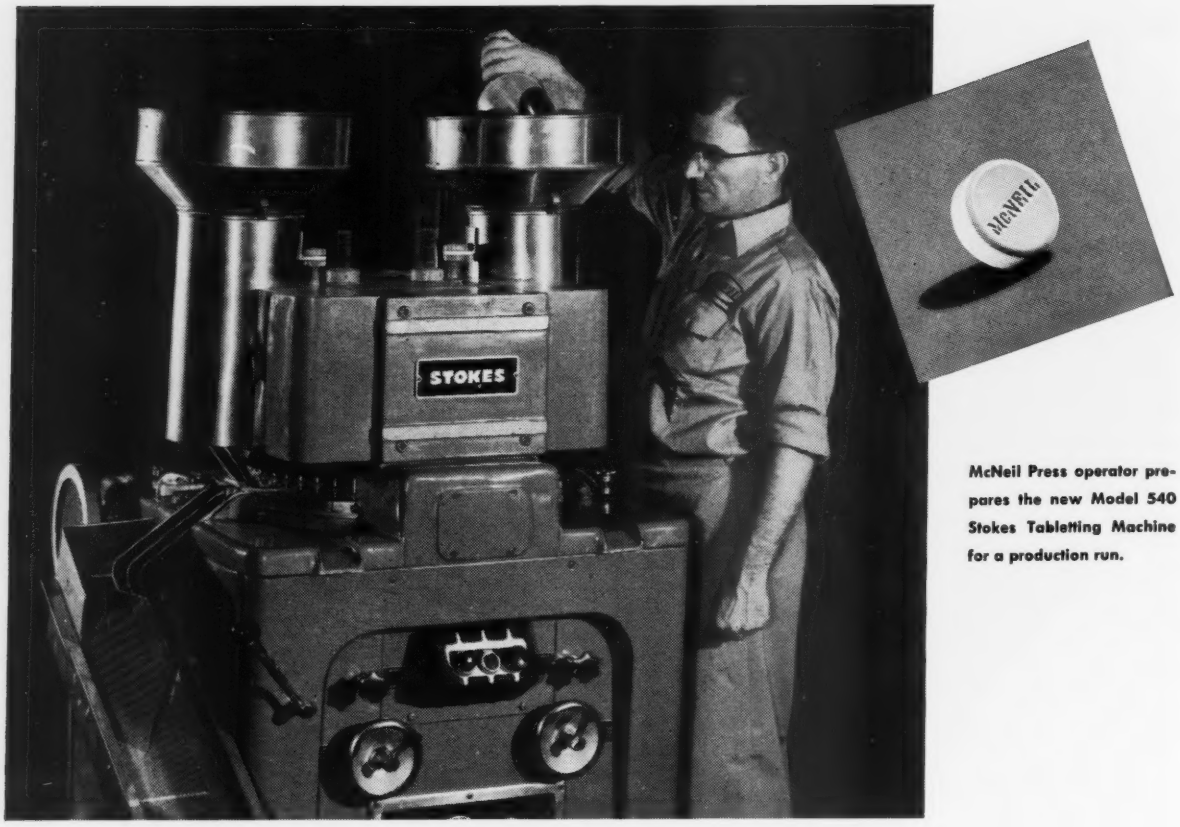

McNeil Press operator prepares the new Model 540 Stokes Tabletting Machine for a production run.

McNeil Laboratories produces Flexin® tablets on new Stokes 540 rotary

Tablets Flexin® Zoxazolamine are being produced on the new Stokes Model 540, 41-station machine at the McNeil Laboratories, Inc. plant, Phila., Pa.

Flexin®, an original McNeil Specialty, is used as a lissive agent in the treatment of musculoskeletal disorders and neurological diseases. The tablets are $^{13}/_{32}$" in diameter—embossed and scored.

The Stokes Model 540 is fast, precise and smooth operating. It is the easiest machine to set-up and adjust that has ever been developed for tabletting. All controls and adjustments are readily accessible on a single panel within easy reach of the operator. Centralized pressure lubrication, greater overload protection and conservative output ratings contribute to long, dependable production life.

Find out how the new Stokes Rotary Tabletting machines can save on your own production. Write or call your nearest Stokes office.

Pharmaceutical Equipment Division
F. J. STOKES CORPORATION
5500 Tabor Road, Philadelphia 20, Pa.

STOKES

Management Forum

By FRANCIS CHILSON
INDUSTRIAL CONSULTANT

Making Packaging Materials

Many firms still make some of their own packaging materials and do some of their own printing. (I do not regard imprinting of code numbers and dates on labels and cartons as printing in the sense of actually making finished paper packages.) Not one of these firms can hope to justify the practice on an economic basis. The manufacture of all kinds of packaging materials:—glass, tin, plastics, collapsible tubes, set up boxes, cartons, labels etc., is individually and collectively a highly competitive business. Firms in this business can make money only by volume operations—keeping all their machines going all the time—; they can make money only by keeping overhead low; by volume buying of raw materials; by using the best and highest speed machinery they can obtain or invent.

When a finished product manufacturer makes any of his packaging materials, he makes only enough to cover his production requirements. This means that his equipment is idle a large part of the time if it is modern high speed equipment; and, if it isn't, he can't possibly meet competitive prices if his costs are accurately calculated. To absorb some of the overhead created by these sideline departments some of them take on outside jobs. Here too they are up against professional competition and unless they are willing to cut prices and ignore profits they haven't a chance competitively.

I know a manufacturer who once made his own collapsible tubes. When the tube company was established originally, it was established as a tube company and was operated as an entirely independent outside investment on the part of the manufacturer and his family. The company in time came to be a dominant factor in the tube industry. Its selling expenses were virtually nil; administration and bookkeeping were simple and inexpensive. Workers were paid the going rate in the industry without a lot of expensive fringe benefits. The company made money—lots of it.

Then the manufacturer decided to sell the tube company to his finished product company. So it was done. Immediately the new dependent subsidiary had to adopt the parent company's fringe benefit plan which added more than a half a dollar per hour to its payroll cost. It was forced to adopt the parent company's elaborate bookkeeping, billing and clerical system, which shot the overhead up to hell and gone. The result? The tube company's profits during the first year of operation as a department of the major corporation shrank two-thirds in spite of increased volume. In a few years the tube company had shrunk to unimportance and what was left of it was sold.

As I mentioned in this column before even so large an outfit as Procter and Gamble found it could not continue printing its own box labels in spite of the fact that it uses countless millions a day, so the print shop was discontinued. Some time ago I was retained by the Scott Paper Co. (toilet tissues and towels) to revamp their packaging methods. In spite of the fact that Scott reckons its output of rolls of toilet tissue and towels, not in millions annually, but in hundreds of millions, it did not then and does not now print its own roll wrappers. The thought occurred to me at the time that here was an ideal application for super high speed Chambon presses, since then only three different brands of roll paper were made. This meant that once a press was set up it could run indefinitely without a copy change. A very detailed economic study of the project failed to prove sufficient potential economy to justify the cost of the equipment and the space required.

The moral of this is, if you are a drug or cosmetic maker. Stick to your own knitting.

Exporting

Time was in the drug and cosmetic industry when nobody gave much of a damn about export business. The majority of firms were not in it at all. Those who were usually exported only to the Central and South Americas. The volume was limited and generally regarded as a damn nuisance, particularly on the part of

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Because much of the initial research on gas (ethylene oxide) sterilization originated at American Sterilizer, growing numbers of AMSCO-developed installations have been serving production and processing industries for more than eight years.

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PRESSURE STEAM

DRY HEAT

If any sterilizing process is or should be a factor in your product . . . outline your problem to us. We can help you!

SCIENTIFIC DIVISION

AMERICAN STERILIZER
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production managers who had to run special sizes in small runs and who had to keep special stocks of foreign language labels and cartons. The export manager was usually some mousy little Puerto Rican, Mexican or Spaniard, who was regarded as completely unimportant—somewhat on the level or a chief clerk. Occasionally he made trips to the southern countries. He operated a small and unimportant empire of his own and few in the organization really knew what was going on in the export department and fewer still gave a damn. Because of this attitude some export managers were able to feather their own nests very handsomely. I know of three important companies whose export managers turned out to be crooks. (Only one of them was sent to jail.)

But since the war the attitude of the drug and cosmetic industry has changed. We realize the importance of export business and we are beginning to learn that if it is handled properly it can be very profitable. There was a time when currency restrictions created a barrier that nobody even wanted to try to hurdle. Currency restriction still obtain but there are ways and means of getting profits out. But what is far more important than immediate profits is the opportunity afforded to participate in the economic growth and development of these economically virgin countries. In exporting the future is far more important than the present.

But foreign countries will no longer stand for exploitation as such. They want an economic stake in the development of their own countries. Therefore the intelligent way to develop an export business is to establish foreign corporations and invite local capital to participate. Some far sighted American companies allow local capital to participate to the extent of fifty percent. I have heard of some who will take even a minority interest in order to establish a firm foothold in a new country. Foreign agents, if they are competent, are eager to participate in the capitalization of local companies established by their clients. Initially their profits are greater than through the usual agency arrangement but what is more important they have an inducement to work harder.

How Little We Know

The late Dr. Daniel Morehouse, for many years president of Drake University, used to advance the proposition that ignorance increases geometrically the more one knows and, conversely, the less one knows the more knowledge he possesses, or in other words, the greater the ratio of his knowledge to his ignorance.

He used to tell his students that each sphere of knowledge was surrounded by the unknown and that the greater the sphere of knowledge possessed by any given individual, the greater his contact with the unknown, since, geometrically the surface of a sphere is 4 times Pi R squared. He used to illustrate his proposition by pointing out that a person of little learning might be considered as having a sphere of knowledge the size of an orange. He therefore would regard himself as learned because of the relatively small surface area of his sphere, i.e., his contact with the unknown. Another person might have a sphere of knowledge the size of a grapefruit. Because of the greater surface of his sphere he would be more aware of the things he does not know than the first person. Still another person might have a store of learning equivalent to the size of a basketball. Because of the enormous increase in the surface area of the sphere in contact with the unknown this person, though he might be regarded as a genius by the other two, would be aware that his learning is insignificant in comparison with the unknown.

It is a pity that there are so few Professor Morehouses in our schools—men who can illustrate a point with apt and vivid analogies which never are forgotten by intelligent students. For many years I have had a hobby of asking successful men to tell me how many teachers in elementary school, high school and college had an important and memorable influence on their lives. The astounding thing is that so many say none. Some say three or four. A few seven or eight. I met only one man who said ten. I was fairly lucky for I can remember—and remember with undying gratitude—five.

This is I think a hell of a commentary on the calibre of American educators and the quality of American teaching methods. Our schools are full of dead-heads and incompetents and that explains why we are so short of first class scientists in all categories; it explains why so few so-called educated people cannot read well, write well and speak well—and who know so little about so much that concerns their daily lives.

Mergers

The Federal Trade Commission is beginning to look more sharply askance at willy nilly mergers. By this I mean mergers that do not make sense. As for instance when a well-known pharmaceutical firm bought a water ski company.

Apart from holding companies, which are established only to maintain financial control of a variety of companies, no merger makes sense unless the acquisition in some way strengthens the parent company. Among the elements of strength are: better control of raw material sources and prices (apart from packaging materials); acquisition of new products which fit the line of the parent company; acquisition of additional volume to fill excess plant capacity; acquisition of related companies in somewhat similar fields that can be made to fit existing organizational, management, psychological and policy patterns.

The attitude and psychology of the parent company is of dominating importance. If the special management or marketing requirements of the new acquisition does not fit that of the acquiring company trouble is bound to ensue. And one does not have to go far from ones own bailiwick to encounter trouble in managing new acquisitions. I have mentioned before the acquisition of cosmetic companies by pharmaceuti-

cal companies during the depression years. Without exception every one came a cropper because pharmaceutical management, particularly marketing management, could not learn the psychology of approach that dominates the cosmetic industry.

Yet these industries are part and parcel of the overall chemical industry. Drugs and cosmetics are distributed in the same wholesale and retail channels. Only a very few firms have succeeded in making the amalgamation and usually these firms started with specialties in both categories long before the depression. Bristol Myers is a good example.

When they cannot be obtained in the right quality and quantity, it is natural for drug and cosmetic companies to make some of their own chemicals. Usually such operations are initially on a very small scale with little thought of general exploitation. Presently it becomes known that a particular drug or cosmetic company can make some unusual chemicals and external sales naturally develop. This type of marketing is technical and usually is done by chemists so there is little sales psychology involved. You can either make a particular chemical at a price or you can't, and if you can't you can't sell it. Bulk marketing is as simple as that.

Some companies grow by acquiring other companies in their own industry. That is all to the good and very often it means the salvation of a small company that lacks the capital to stay in the fight, or lacks the capital to do the research which the development of its own products require.

Not all mergers are to the benefit of both parties even when they take place within the industry. Officials of big companies frequently become over-enthusiastic about the potential of small companies which they have an opportunity to buy. They delude themselves by assuming that they can enjoy all the profits of the small company without any additions to marketing, administrative and research expenses. They have a habit of looking at the profits only without considering the ratio of overhead to sales which made those profits possible.

Often the small company has no fringe benefits beyond the legal minimum requirement. Even when the small company is allowed to operate independently, the payroll rates, fringe benefits and policies of the parent company will soon be forced upon it. As a matter of course (which the controllers will see to) the elaborate bookkeeping and clerical system of the parent company will be forced upon it. Everything must tie in. The new acquisition may not be unionized and hence may have lower labor rates than the parent company. But not for long!

The only sensible way to compute the value of a new acquisition is to calculate what its profits would have been if it had had to carry the same overhead as the parent company.

Vibrating Screen Separators

New 30" diameter vibrating screen separators in 1, 2 and 3-deck models for the process industries have been announced by the Southwestern Engineering Company, 4800 Santa Fe Avenue, Los Angeles, Calif. The new models round out the company's separator line—giving an intermediate size between the 18" and 48" diameter units.

The new 30" model operates on the same three dimensional gyratory principle as other SWECO separators. It is constructed of carbon steel or type 316 stainless steel and employs a totally enclosed 60 cycle, 3 phase, 1200 RPM, 1/2 HP, 220/440 V. motor. Explosion-proof motors, 50 cycle and 550 V. motors are also available.

Compression Coating Machine

A new high speed Colton compression coating machine which applies dry coatings to capsule-shaped tablet cores at rates up to 925 tablets per minute is available from Arthur Colton Company, 3400 E. Lafayette, Detroit 7.

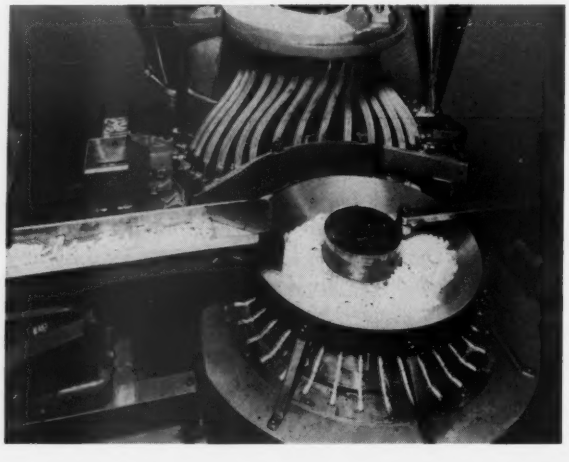
The capsule-shaped cores are handled by a new slow-transfer feeder assembly that is mounted on a standard Model 232 Colton Compression Coating machine. The cores are fed by a Colton No. 30 tablet duster into a metal hopper in the feeder. The cores fall through collector ring holes below the hopper and travel down V-grooves in a conical magazine feeder into slots in a core positioning ring. The collector ring, magazine feeder and core positioning ring rotate as a unit.

The magazine feeder is vibrated by an external vibrator assembly to assure positive feed of cores to the ring. The cores are picked up from the core positioning ring one-at-a-time by vacuum pickup nozzles. These nozzles are attached to a special chain driven by the press die table. The cores are deposited by the nozzles in the dies which have been partially filled with a lower layer of dry granular coating material.

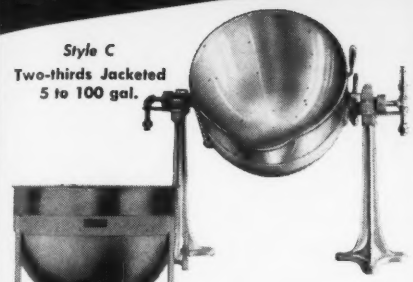
The top layer of coating material is fed over the core in the die before it reaches the pressure rolls where the coating is compressed onto the core.

Like other Colton Model 232 compression coating

Colton's New Slow-transfer Feeder

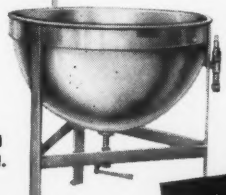


COOKING KETTLES

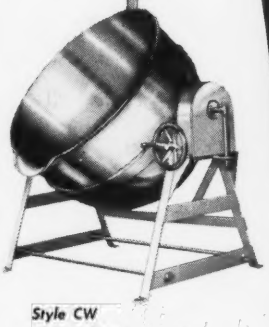


Style C
Two-thirds Jacketed
5 to 100 gal.

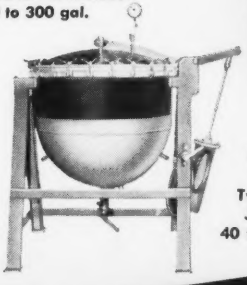
Style A
Two-thirds Jacketed
5 to 500 gal.



Style B
Full Jacketed
10 to 300 gal.



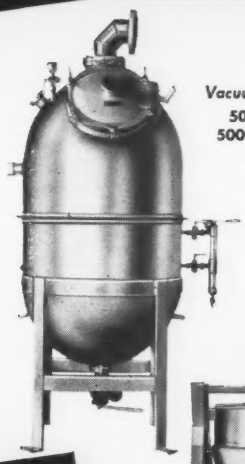
Style CW
Two-thirds Jacketed
80 to 300 gal.



Pressure Kettle
Two-thirds Jacketed
40 to 200 gal.

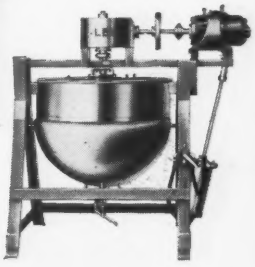
MIXING AND BLENDING UNITS

CW3T
Center-line Scraper Agitator Kettle
80 to 300 gal.



Vacuum Pan
50 to
500 gal.

D3T
Center-line Scraper Agitator Kettle
25 to 300 gal.



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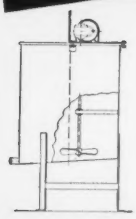
Quick Cooling Pan
50 to 200 gal.

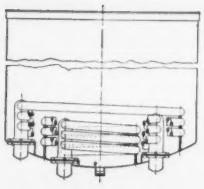
Individually designed for a specific processing operation and available in a wide range of sizes to fit your exacting requirements, Lee corrosion-resistant equipment is built to give you long years of peak performance with minimum maintenance.

Descriptive bulletins are available for any or all of the above units. Write for them today and discover how Lee can help reduce *your* processing costs.

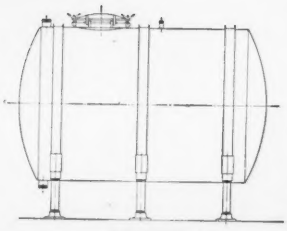
MIXING, COOKING & STORAGE TANKS



Mixing Tank
25 to 500 gal.



Pulp Tank
500 to 2,000 gal.



Storage Tank
100 to 5,000 gal.

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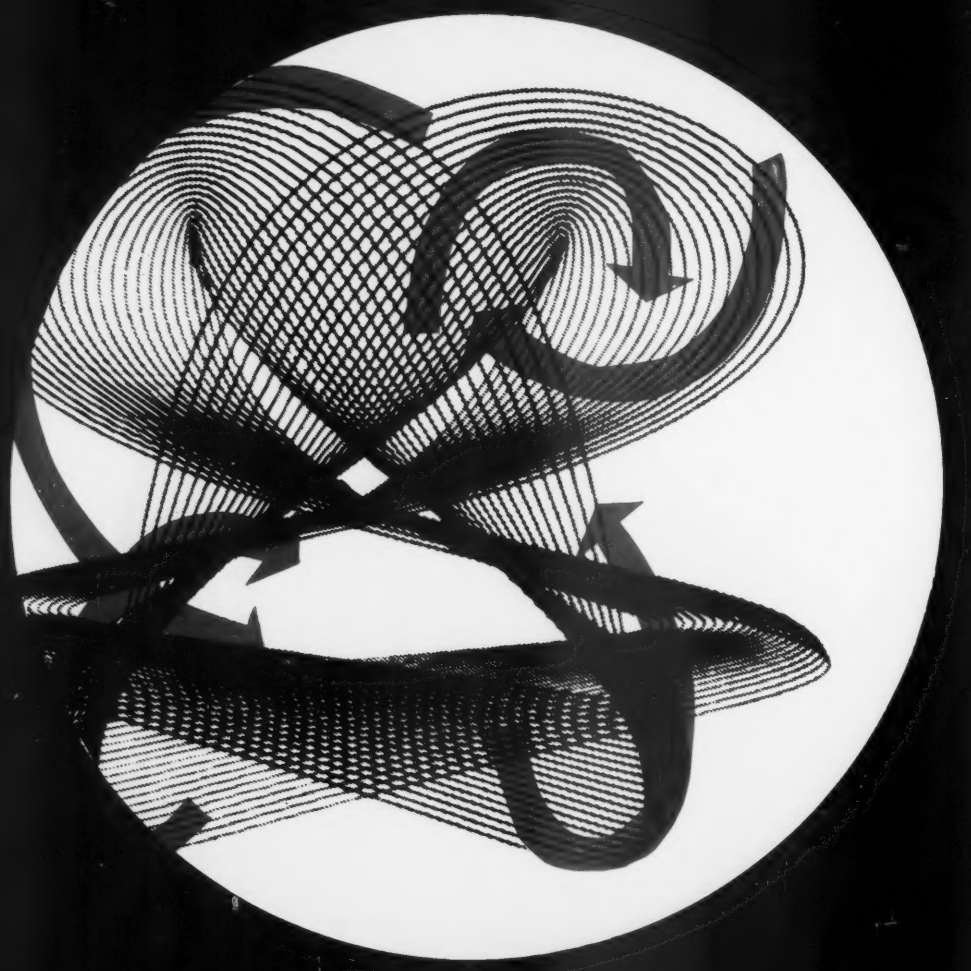

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machines, which dry-coat round tablet cores at rates up to 1,000 tablets per minute, this new machine will not produce coreless tablets and provides for positive centering of the cores within the coating material. Metering of the coating material layers assures accurate control of coating thickness as well as preventing the production of coreless tablets.

The new Colton compression coating machines for handling capsule tablet shapes are now in full production in pharmaceutical plants and more are in the process of manufacture to fill new orders.

Columbia College Gets Tablet Coaters

Columbia University College of Pharmacy has added two compression coating tablet machines to the equipment already installed in its Industrial Pharmaceutical Manufacturing Laboratory.

One machine was received from the F. J. Stokes Corp. of Philadelphia and is the company's latest production model press coating machine capable of yielding 500 tablets per minute. The other press was obtained from the Fitzpatco Corporation of Chicago and is the most recent Monesty Dry Cota producing 350 tablets per minute.

The College of Pharmacy will use these machines as research and teaching tools in connection with the courses offered in its graduate program in manufacturing pharmacy. Investigations into the development of new uses and research that will aid in the improvement of the process of press coating will not be a major part of the graduate research in manufacturing at the school. Research work on compressed coated tablets will be done under the direction of Professors Leonard Chavkin and Joseph Kanig.

Changeable Can Mixers

A new series of heavy duty changeable can mixers, precision engineered to develop the greatest shearing and dispersing action in mixing paste materials, has been developed by Charles Ross and Son Company, 148 Classon Avenue, Brooklyn 5. Available in sizes from 1 to 150-gallon working capacities, they employ intensive double planetary mixing action. Each stirrer revolves on its own axis, while both are revolved at a slightly slower speed around can.

Uncle Dave Goes to Town

It was about 1909, I think, that Uncle Dave Whitlock made his first trip to a big city. A very big city by Uncle Dave's standards—about seventeen thousand people. "God a'mighty!" Uncle Dave told us afterward. "I never saw so many people. Minded me of a swarm of bees." Up to that time Uncle Dave had never been more than twenty-five miles from the farmhouse in which he was born. There was no need for him to travel. But on this occasion he had to represent the family at the funeral of an aunt. Seventy-five miles away! Had to go by train of course. Couldn't drive horses that far. It was like a trip to the moon. Besides there wasn't time to drive that far. As Uncle Dave said, "The old bitch'd be planted before I could get there."

Uncle Dave's trip caused intense excitement in the little hamlet. He was told he ought to carry a pistol in his belt just in case. He was advised to watch out for "them city gals." It was known that they were all wild women. It had even been rumored that some of them wore face powder!

But Uncle Dave went on with his preparations with his characteristic calm. He had a new blue Sears Roebuck suit and he bought a new pair of patent leather button shoes with gray suede tops. He also bought some new celluloid collars and cuffs and Ma washed and ironed several white shirts for him. When he was dressed up he really looked a dude. Ma kissed him good bye and said she didn't want him going into saloons and drinking rotgut.

Pa and I drove him to town to catch the morning train, but, in spite of what Ma told him, Uncle Dave insisted on stopping at the Half Way House for a couple of slugs of liquor. He was feeling pretty good when he came out. You could see that. Both pockets of his coat contained pint bottles of whiskey. "Just in case I get thirsty on that dang train," he told Pa.

Pa told him, "For Lord's sake, Dave, don't go in to Aunt Lizzie's with whiskey on your breath 'cause she'll get right up out of her coffin and blast the hell out of you!".

I admired Uncle Dave getting on that train all alone and going off into the far places. Like Admiral Peary setting off on a trip to the North Pole that we had heard tell about.

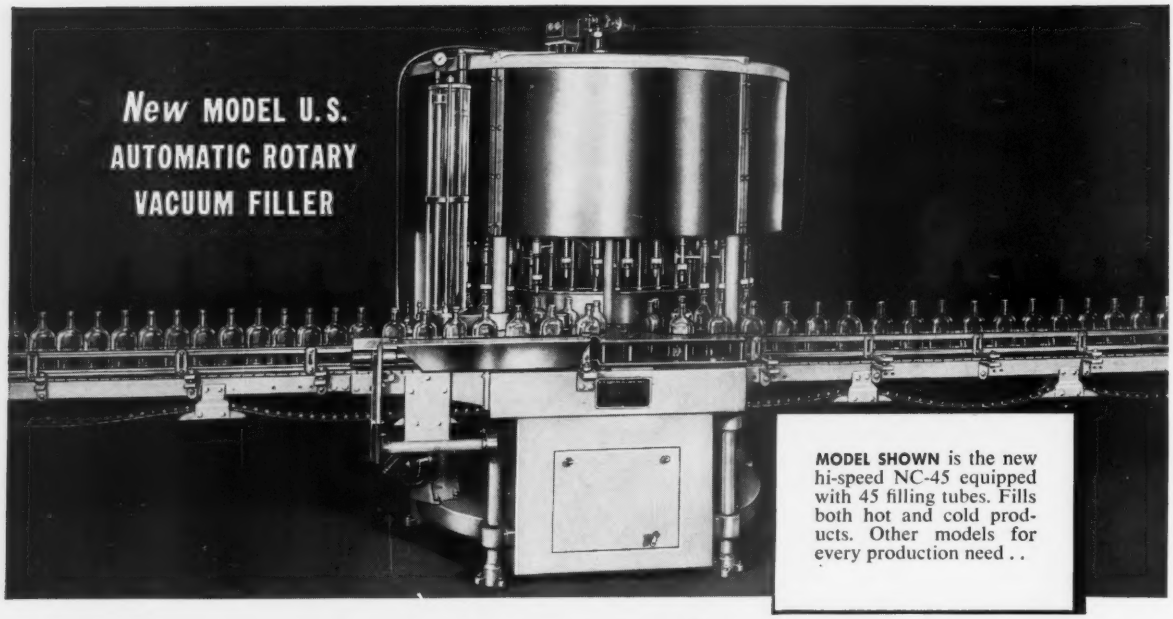
From all accounts Uncle Dave had himself a time all right. But the high point of his trip came a short time after he arrived at Aunt Lizzie's home.

We were all sitting around Bill Haley's store a few days later waiting for the mail to be sorted, when Uncle Dave came back. He came home on the mail stage which met the train at the rail head. He immediately became the center of attention. Everybody asked questions at once. Uncle Dave told all sorts of things, but the apex of his adventure as a traveler came shortly after his arrival in the big city.

"I kept gettin' more uncomfortable by the minit," Uncle Dave related. "I just had to *go*. So finally I said I would look around outside for a bit. So I went round back of the house and there wasn't an outhouse anywheres! I always knowed city folks was queer but not that queer. I got to feelin' like I was goin' to bust. So I went back inside and told Uncle Charlie I just got to *go* somewhere *quick!*

"So he took me into a little room about the size of a pantry and it had a white china bath tub and a white china wash basin and a little white china jigger with a kind of wood ring onto it that looked like a horse collar. I thought to myself, 'I always knowed city folks was crazy but this does beat all.' Imagine havin' the outhouse *inside* the house! And everything white china too!"

Uncle Dave never traveled after that. He had no need to. He had seen the wonder of the world.



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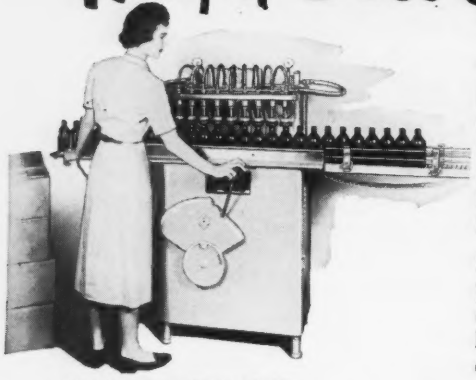

MODEL B-49 STRAIGHT-LINE VACUUM FILLER for liquids and semi-liquids. With or without discharge conveyor. Contact parts stainless steel, or plastics on order. Adjustable for AGST to gallon size finishes. Send for the Model B-49 Bulletin.

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MODEL B-2 VACUUM FILLER. Continuous production, filling two containers at a time. For liquids and semi-liquids. Automatic product supply. Vacuum adjustable and flow-regulated. For containers up to 4⅛" dia. Send for Bulletin B-2.

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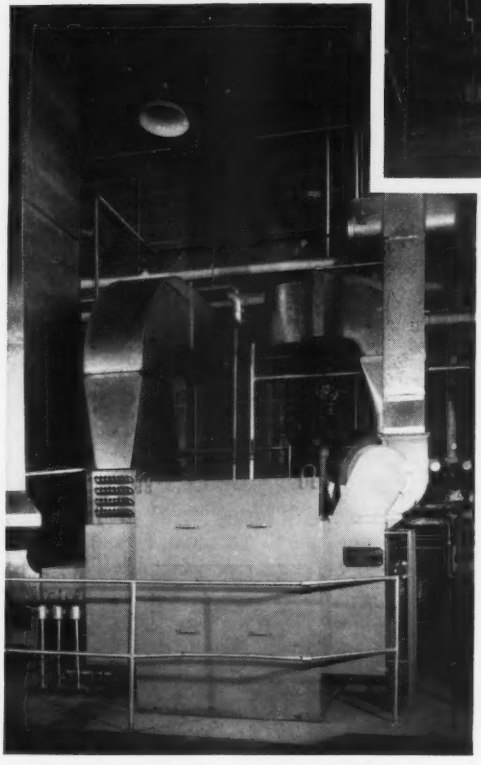

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Lectrodryer

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Trade Literature

Gramacidin

S. B. Penick & Company, 60 Church Street, New York 8, has published a 20-page review of recent clinical literature on Gramacidin, which is the constituent which accounts for the accepted therapeutic activity of tyrothricin. Its use in respiratory and dermatological infections is gaining momentum as the result of recent clinical reports. Gramacidin with neomycin provides a potent chemotherapeutic effect against a wide spectrum of most common Gram-positive and Gram-negative bacteria.

New Antistatic

Pennsalt Chemicals Corporation, Department P, 3 Penn Center, Philadelphia 2, has available a booklet on ethylsulfonylethanol, a new chemical with highly effective antistatic properties combined with low toxicity. An unusual combination of properties including miscibility with water and many polar organic solvents, reactivity typical of aliphatic alcohols, and mild humectancy suggest evaluation of this chemical as a base for cosmetic and pharmaceutical properties.

Naxol (Cyclohexanol)

National Aniline Division, Allied Chemical & Dye Corporation, 40 Rector Street, New York 6, has issued Technical Bulletin I-20 on Naxol (cyclohexanol), a 32-page booklet containing the most complete data yet assembled on this unusual intermediate. It contains ten pages of physical and chemical properties, and describes and illustrates all principal reactions. In addition it provides eleven pages of suggested uses in various industries including pharmaceuticals and perfumes.

Physical Properties

The new 1958 Physical Properties booklet (F-6136) is now available from Union Carbide Chemicals Company, 30 East 42 Street, New York 17. This 28-page booklet presents physical property data on more than 350 organic chemicals. Fifty new chemicals introduced by Carbide since the previous edition are featured. Viscosity index improver D and Crag Sevin experimental herbicide are two of the new products described in the section on chemicals for special applications.

Glass Volumetric Apparatus

A newly revised manual on The Care and Handling of Glass Volumetric Apparatus, is available from Kimble Glass Company, Toledo 1. The 24-page booklet is divided into four chapters and is complete with illustrations, tables, and charts of prime value to the laboratory worker. The four major segments cover systems of weights and measures, capacity tolerances, standard temperatures determination of capacities, rules for manipulation of glass volumetric apparatus and delivery characteristics of burets and pipets.

Medical Indigence

An Examination of the Concept of Medical Indigence, by Odin W. Anderson, Ph.D., and Harold Alksne, M.A., is No. 2 of the Research Series of booklets issued by the Health Information Foundation, 420 Lexington Avenue, New York 17.

Corn Oil

Corn Oil, a 20-page illustrated booklet, is available from Corn Industries Research Foundation, 3 East 45 Street, New York 17. This oil has uses in this industry, among which is as a carrier for vitamins.

(*Continued from page 741*)

tion in which there is neither up nor down for the passenger—and consequently no way for his semi-circular canals to maintain the sense of balance. It is perfectly possible that this will be an utterly incapacitating experience for a human being, creating a "space-sickness" which will make ordinary motion-sickness seem like a pleasure by comparison.

Oddly, however, this question—which is not very amenable to study in the gravitational field of the Earth—appears to be nearly resolved. Animal tests (with mice, in the U. S., and with Muttnik in the USSR) do not suggest that weight-lessness is actually so drastic an experience. Some very difficult and ingenious experiments in jets with human volunteers, conducted by Dr. Siegfried Gerathewohl (USAF School of Aviation Medicine, Randolph Air Force Base, Texas), show that about half of the human race will probably actually enjoy weightlessness, though it will certainly confuse them and tire them until they get used to it; about 25 per cent will be substantially indifferent to the experience; and the other 25 per cent will become horribly sick. And even some percentage of this last quarter may be amenable to standard motion-sickness drugs such as meclizine; the intractable remaining fraction, however, will be permanently invalided out of space travel.

A more difficult aspect of orientation is purely psychological: that of confinement. This problem, as Dr. Haber points out, is comparable to that of the crew of a plane which is flying continuously around the world without touching down. In such crews, and in the crews of submarines forced to remain under water for long periods, fatigue and apprehension build rapidly, and begin to take their toll in terms of delayed reflexes, irritability, and just plain bad judgment. In a submarine, as the Navy well knows, there is no such thing as a minor mistake, and a spaceman can afford no mistakes at all. Haber estimates that, coupling this factor with weightlessness and with the conditions of almost complete restriction of movement which would obtain, 24 to 30 hours would be the longest tolerable tour of duty under presently imaginable conditions.

Decompression, the fourth problem, is well known to divers, as the phenomenon of the bends. Sudden pressure drops cause the nitrogen dissolved in the blood to come out of solution in the form of small bubbles. This phenomenon, also known as caisson disease, can be rapidly fatal; it permanently crippled the builder of the Brooklyn Bridge.

In space, caisson disease would arrive explosively, in the form of a puncture of the hull of the vessel by a meteor. Were the rupture serious enough, the air pressure might well drop to nothing in a few minutes or seconds, which would almost surely be fatal to all aboard.

A few—a very few—ground rules for coping with the problem are now known. One of the simplest is to

(*Continued on page 824*)

Ask the man from Vanderbilt about VEEGUM for making drugs and cosmetics attractive to buy and use

Veegum is a remarkably versatile physical conditioner for your lotions, tablets, pastes and creams. It gives them a look and feel of quality and a smooth, appealing texture that attracts sales and invites use.

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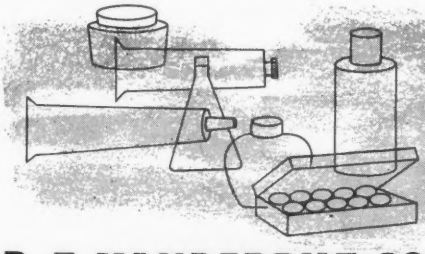

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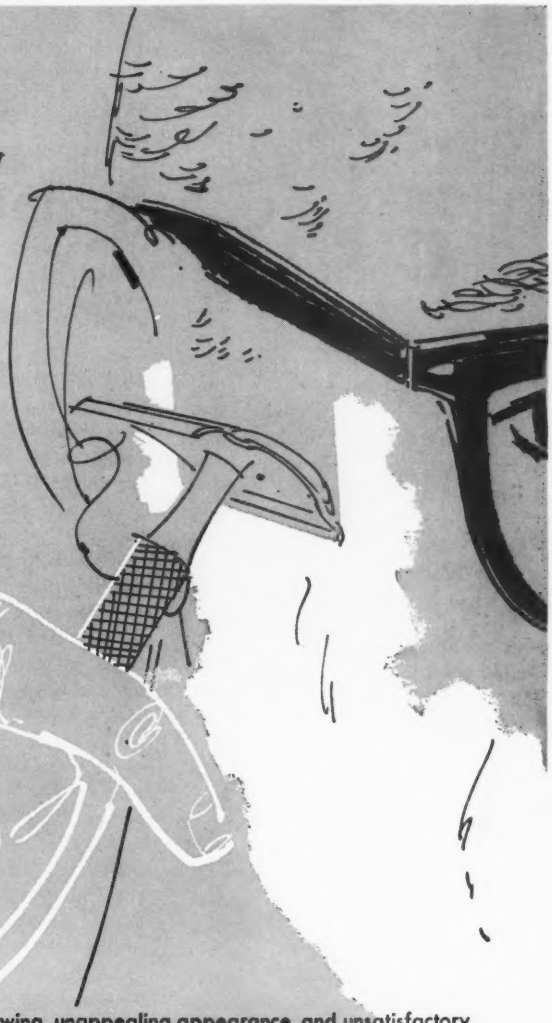

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Compounder's Corner

Motivation

Currently, motivation is the big word in designing advertising, and like any self-respecting chemist I am made queasy by the word. The huckster psychologists are trying to make us believe that they can develop techniques that will make people, even against their desires, buy a product, and they may be right; even before they called it motivation, advertising people so deadened us by repetitive pitches that we could think only of their product at point of purchase. None of this, however, distinguishes between the first impulse to buy and the repeat sales potential. All of this motivation approach seems to me to disregard completely the question of product merit. Once you persuade the customer to buy your product, then the product must do the permanent selling job. If the product is poor, the customer is lost; if the product is average or mediocre it engenders no brand loyalty and the cost of selling has to remain high. Only if the product is demonstrably superior will it develop selling momentum of its own and make the advertising expenditure a profitable thing.

Not so oddly, then, I return to my theme song: spend money for research to develop products of demonstrable merit, so that high advertising costs required to lure new customers will be justified. Ethical pharmaceutical manufacturers, as their income statements show, know the value of effective research; distributors of proprietaries and cosmetics, with few exceptions, are still reluctant to do an adequate job.

Polyvinylpyrrolidone

Polyvinylpyrrolidone, PVP is fully described in a booklet just issued by the Antara Chemicals Division of General Aniline & Film Corporation. Three commercial types of the material are available: K-30; K-60; K-90, characterized by their degree of polymerization. The K-30 grade has an average molecular weight of 40,000 and is offered as a white powder containing 95 per cent of active ingredient. K-60, a 45 per cent aqueous solution, has an average molecular weight of 160,000 and the K-90, in 20 per cent solution, has an average molecular weight of 360,000. The K-30, in solutions containing less than 10 per cent, has little effect on viscosity and viscosity is not appreciably changed over a wide pH range. The polymer may have considerable influence on the viscosity of organic solvents in which it is dissolved.

PVP, K-30, is readily soluble in cold water, 60 per cent solutions still flow, and solubility is limited only by the viscosity of the solution. It is freely soluble in many organic solvents including alcohols and chlorinated compounds and when anhydrous will dissolve in ketones, dioxane and toluene. K-30 is directly soluble in chlorfluoroalkanes containing the $-CHX_2$ group and in the presence of alcohol will dissolve in several other propellants.

Dried unmodified films of PVP are clear, transparent, glossy and hard from any solvent system. Compatible plasticizers modify the film without affecting clarity or luster. Tack and brittleness may be contolled by CMC, cellulose acetate, and shellac; dimethylphthalate is less effective, while the glycols tend to increase tackiness. In hair fixative mixtures, lanolin derivatives are effective film modifiers. PVP is compatible in solution and as a film with Carbowax, gum arabic oleyl alcohol, cetyl alcohol, diethylene glycol oleate and ethyl cellulose, in addition to compounds previously mentioned. Some modifiers that give cloudy films may be useful. These include Ucon oils, karaya, tragacanth, beeswax, olive oil, castor oil, mineral oil.

PVP powder is hygroscopic, but otherwise completely stable; aqueous solutions should contain a preservative to prevent molding. Acute toxicity is extremely low and PVP is non-toxic orally, by inhalation or intravenous or intraperitoneal injection. On the skin it is not a primary irritant or sensitizer, is non-antigenic and will not cause skin-fatigue. It does not cause irritation of the eyes.

In cosmetics, PVP has been found extremely useful in a number of applications. Aerosol hair sprays and liquid grooming preparations contain 2 to 5 per cent, and they may be formulated with plasticizers, modifying resins, lanolin derivatives and perfumes. PVP displays unusual affinity for the hair. The transparent film adheres well and does not flake off. The PVP is adsorbed by the hair and is not easily removed completely by rinsing. The addition of about 3 per cent of the polymer to color hair rinses tends to make dye application more even and improves adherence. Shampoos benefit by the addition of PVP in terms of foam stabilization and better soil removal. In shaving preparations, lather is stabilized, wetting action is improved and irritation reduced. In makeup preparations, PVP as a film former improves adhesion and reduces penetration by oils and also has humectant properties for skin moisturizing. PVP has also been utilized with advantage in hand lotions, massage creams, mascara, cream rinses, etc.

In Pharmaceuticals, PVP can function as a tablet binder and controls viscosity in liquids; it may be useful in reducing irritation in ophthalmic products. Topically, its detoxifying action is useful.

Atropine Stability

The rate of acid hydrolysis of atropine has been measured by A. A. Kondritzer and P. Zuirblis (*J. Am. Pharm. Assoc. Sci. Ed.* 46: 531,1957) in aqueous solution, and the activation energy and frequency factor calculated from Arrhenius plots. As expected, the hydrogen ion catalyzed hydrolysis of atropine is slow, compared to that for the hydroxyl ion catalysis. *(Continued on page 809)*

Romance!

In the cosmetics industry, romance is probably the greatest single sales-motivating force. And the cosmetics chemist knows that fragrance plays a dominant part in her selection of cosmetics.

That's why so many manufacturers who are meticulous about fragrance use Verona extenders and developers to bring out the latent brilliance of the compound . . . *and save money in the process!*

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Above pH 4.5, the predominant catalytic reaction involves hydroxyl ion; below pH 3, the predominant catalytic reaction involves hydrogen ion; while between these two regions, both ions contribute to the hydrolysis.

The pH for maximum stability of atropine in sterile aqueous solution varies between 4.11 at 0° and 3.24 at 100°.

Emocithin

Emocithin, already in wide use in Europe, is the development of W. A. Scholten's Chemische Fabrieken, Foxhol, Netherlands, and is now being distributed in the United States by Morningstar, Nicol, Inc.

Emocithin produces W/O emulsions which will not separate at temperatures up to 200°F (by ASTM Steam Emulsion Test D 157-36). These emulsions are tasteless and odorless and their suitability for food, pharmaceutical and cosmetic use has been established.

In pharmaceutical and cosmetic applications Emocithin can be used to formulate aqueous medications in the form of emulsions in oil to extend their absorption period; to incorporating water soluble flavors, colors, or other ingredients in fatty cosmetics; for improving the organoleptic properties of orally administered medicinals; and to make liquid W/O cosmetic emulsions.

Other application possibilities include improved anti-staling agents for baked goods, extending lubricating waxes, adding water soluble corrosion inhibitors to lubricating oils, stabilizing the water in fatty pet foods, and carrying small quantities of water into internal combustion engines (with the gasoline) for better performance.

Emocithin is a semisolid available in both food and industrial grades and is described in U. S. Patent 2,552,706. It is easily incorporated in oils, fats and waxes by simple warming and blending techniques. Quantities used range from 1/10 to 2 per cent of the oil content.

Apart from the unique heat stability of the emulsifier, the water-in-oil emulsions obtained with two per cent of Emocithin are uniform and fine-grained. Its ability to form fine dispersions makes Emocithin ideal for dispersing dyes and pigments in cosmetics in paints, where it will counteract pigment settling.

Peroxide Bleaching

The bleaching of hair is usually done by means of an alkaline solution of hydrogen peroxide containing 20 volumes of oxygen. Weaker solutions will also give good results; ammonia is the alkali usually used and is added to the peroxide just before use. The alkali liberates oxygen which does the bleaching and also swells the hair so that the oxygen can act on the pigment within the hair shaft.

An effective bleach liquor is obtained by the combination of hydrogen peroxide with an alkaline detergent solution, which promotes saturation and penetration of the hair by the liquor. If long treatment is desired, the mixture of peroxide and detergent can be lathered on the hair and further treatment is not required.

In treating hair with an alkaline solution of peroxide, the bleaching progresses through a number of shades. Black hair first becomes brown, then red and then red gold. The red tone fades and becomes golden blond, yellow and finally white. For a successful bleach treatment, it is important to stop the reaction at the right time by carefully washing the hair. If the peroxide remains on the hair too long, the hair may be damaged and take on an unpleasant color. The peroxide attacks the cystin disulfide linkages that bind the polypeptide chains in keratin. Damage is less in neutral or acid solutions. The peroxide treatment can be dangerous when there are traces of metal salts on the hair, as from a previous dyeing. The metal ions catalyze the oxidation of keratin. Repeated use of a peroxide bleach makes the hair lifeless, dry, brittle and difficult to wave. A peroxide bleach combined with a conditioner gives new luster to the hair.

Milder bleaching results from the use of acid solutions. Although not entirely suitable for complete bleaching jobs, these solutions can be used for lightening the hair. The peroxide solution contains less than 10 volumes of oxygen and is made slightly acid by the use of organic acids. To accelerate the bleaching action, a quaternary or similar cationic compound is added. The quaternary acts as a wetting agent and softener; suitable compounds are cetyldimethylbenzylammonium chloride or quaternary morpholine sulfates such as alkylethylmorpholine ethyl sulfate. The concentration of these compounds in the bleaching solution can vary between 0.5 and 2.5 per cent. The organic acid concentration should not exceed one per cent and suitable acids are adipic, tartaric and glutamic.

The usual peroxide stabilizers are sodium stannate or sodium pyrophosphate and the solution can be stored without decomposition. The solution has a pH value of 4.0 to 4.5.

The lotion can be allowed to dry on the hair without damage and the cationic acts as a hair conditioner. The treatment can be repeated without harming the hair.

—*Indian Soap Journal*, vol. 22, p.56

"MD" on Cosmetics

In an otherwise factually correct article, the medical newsmagazine "MD" discussed cosmetics but still managed to display unnecessary ignorance. Among "leading irritants and allergens" was mentioned tallium salts (sic!). To our knowledge, the toxic thallium salts have not been used in American cosmetic formulation for at least twenty years.

In Vivo Antacid Determination

Although several instruments have been described for the continuous measurement of pH *in vivo*, the equipment assembled by J. W. E. Harrison et al (*J.Am. Pharm. Assoc. Sci.Ed.* 46:519, 1957) for the electrometric recording of pH within the stomach, has the following advantages. (a) The special stomach electrode records in a normal as well as inverted position. (b) The multiple switch arrangement allows studying many patients simultaneously. (c) The addition of the "reference electrode" reduces the possibility of inherent drift within the apparatus. (d) The polyethylene shield of our design prevents contact between the electrode and gastric mucosa.

This study indicates clearly that the apparatus which assembled for measuring pH continuously is applicable for evaluating the *in vivo* effects of potential antacid agents. The results obtained electrometrically check so closely with the results obtained with aspiration techniques that the reliability of the data is assured.

By comparative techniques, four antacid agents have been evaluated, for their effects upon the acidity of the gastric contents. As a criterion of effectiveness the pH range of 3 to 5.5 was chosen since in addition to neutralization, there is assumed to be little or no alteration in the normal physiologic processes of digestion within the stomach within this pH range.

Based upon the data accumulated by both the aspiration technique and the continuous pH recording method, the antacids in decreasing order of their effectiveness were dihydroxy aluminum sodium carbonate, aluminum hydroxide, calcium carbonate, and sodium bicarbonate.

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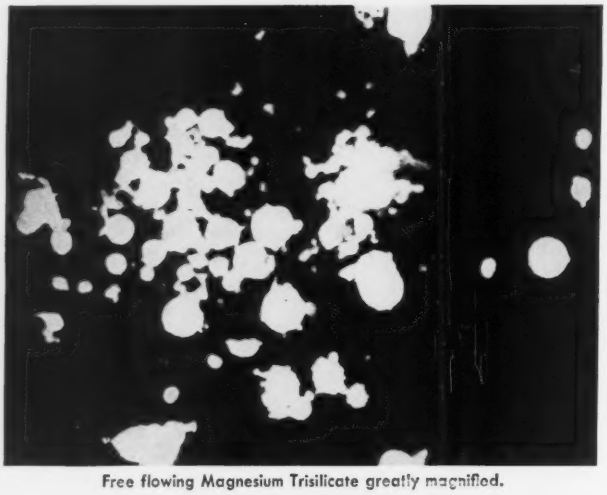

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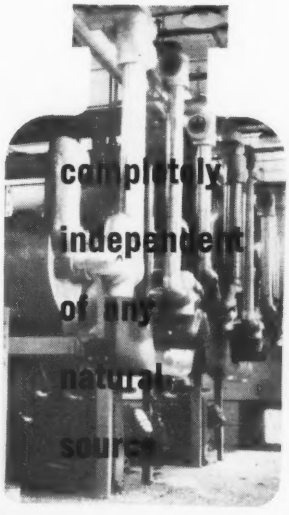

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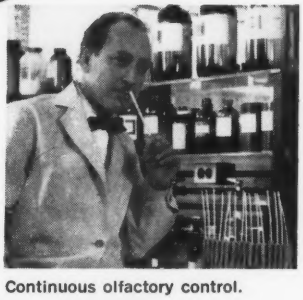

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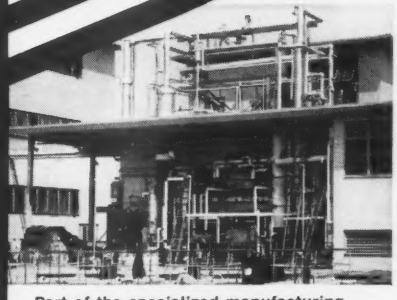

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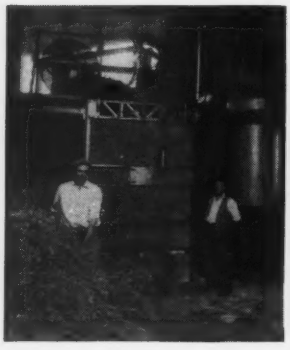

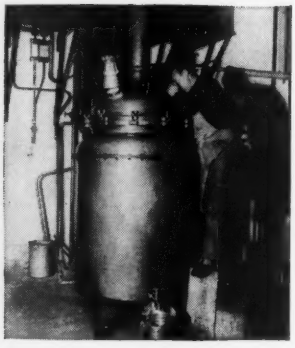

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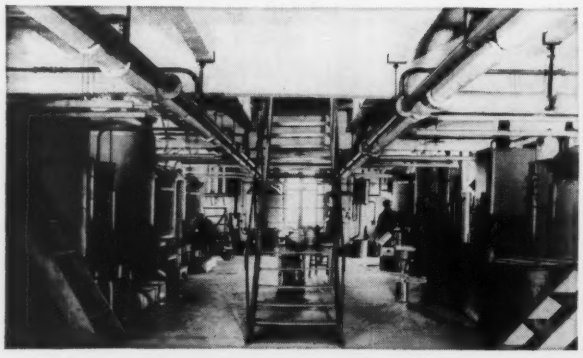
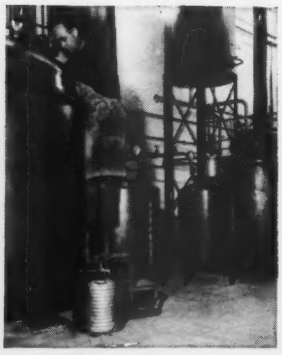

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Skin Research

Waterless Skin Cleansers

More than a year ago, L. Goldman, R. H. Preston and S. R. Scheen, Jr. (*A.M.A. Arch. Dermatol.* 76: 208, 1957) began a study of some of the waterless cleansers in clinical dermatologic practice. To date, 3065 patients have used three of these materials. Cleanser "A" was used by 614 patients; cleanser "B" by 2361 patients, and cleanser "C" by 90 patients.

Modern waterless skin cleansers are classified according to their primary cleansing ingredient: (1) petroleum oil or solvent; (2) soap, ammonia, or alkali, and (3) a system of wetting agents. Some cleansers may be mixtures of 1 and 2 or 1 and 3.

All cleansers selected for this study were classed as wetting-agent type alone or in combination with petroleum oils or solvents.

The following are the basic active ingredients of the cleansers studied:

A—Unknown, wetting-agent system suspected, slight amount of water immiscible solvent.

B—Oil-in-water emulsion of sarcosinates, sulfonates, hexachlorophene, polyethylene liquid petrolatum base, no hydrous wool fat (lanolin).

C—Purified hydrocarbons (oil), fatty acid soap (alkanolamine), hydrous wool fat, propylene glycol, titanium dioxide, carboxymethylcellulose, nonionic type synthetic degergent of fatty amide condensate type, paraffin wax, soap odorant, methyl *p*-hydroxybenzoate, water.

It is obvious that all of the rigid tests for efficiency as an industrial cleanser do not apply for use in routine dermatological practice. The products used in clinical practice must, of course, be efficient, safe, and pleasant to use. The tests selected, then, were only those of mildness, cleaning efficiency, effect on skin pH, and the degree of residual material left on the skin after use.

The relative mildness of soaps can be demonstrated by the seven-hour closed patch test technique of Kooyman and Snyder. Cleanser "C" was found to produce marked irritation. It does not follow necessarily that this artificial testing parallels clinical usage. However, those creams which did reveal mildness on testing did show mildness during clinical usage on normal skin.

Tests of the effect on pH of the skin were done to determine the degree of surface alkalinity induced by the use of 5 gm. of cleanser cream for 30 seconds on the palmar and dorsal surfaces of the left hand. In this series, creams "A" and "B" did not greatly alter the skin pH after 30 seconds of usage.

Product acceptance is important in clinical practice. Cleansers "A", "B," and "C" were white creamy materials and pleasant to use. It was decided to limit the study to the following basic groups of cases: (1) "hand dermatitis"; (2) acne; (3) diaper dermatitis; (4) cleansing routines in fungous infections, especially of the feet; (5) infantile eczema and atopic dematitis; (6) cleansing routines for ulcerations (localized and generalized); (7) as an ointment base for various dermatologic medications; (8) as a cleansing agent for removal of messy and staining ointments, and (9) miscellaneous conditions (shaving, cleansing external auditory canal, etc.).

In the hand dermatitis group, cleanser "A" was used by 390 patients, cleanser "B" by 675 patients, and cleanser "C" by 42 patients. In general, all these cleansers had similar effects. In the active eczematoid eruption phase, the reactions after use were high, 20 per cent. These included burning, increased redness, and increased vesiculation of the erupted sites.

The waterless cleanser, then, has only a limited value in hand dermatitis during the active phases, a somewhat greater value during the dry phase.

The greatest field of interest was in the acne group. Cleanser "A" was used by 210 patients; cleanser "B" by 1453 patients, and cleanser "C" by 46 patients.

Seborrheic dermatitis of the face was definitely aggravated by these cleansers. In most instances, rosacea was likewise irritated. From a cosmetic aspect, the effective cream cleanser was acceptable to the patient with acne.

Cleanser "A" was used by 8 patients with diaper dermatitis, and cleanser "B" by 41 patients. The cleanser was more effective than oils for the removal of feces and encrusted medications.

The frequency of local irritation from the use of cleansers "A" and "B" during the active phase of the diaper dermatitis was 2 per cent.

In infantile eczema and atopic dermatitis, the cleanser creams had limited value, chiefly to remove tar ointment. Cleansers "A" and "B" were almost uniformly irritating on the face. Cleanser "B" was more irritant to the eye than cleanser "A".

Cleanser "B" was used in the trichophytosis treatment program in 145 cases which included eczematized, secondarily infected, and chronic phases. Cleanser "B" was used also in a series of four cases of Trichophyton rubrum infection of the hands. Although cleanser "B" was pleasant and acceptable for use, no definite conclusions relative to its actual therapeutic value could be drawn.

All three cleansers, "A," "B," and "C" had definite value in the removal of tenacious ointments such as tars, zinc oxide, etc. They were definitely more effective than mineral oil for this purpose.

Cleanser "B" was used as a cleansing agent to remove serous and purulent discharges, powders, and ointments in a series of stasis ulcers, pyogenic ulcerations, and cutaneous malignancies with ulcerations. At times, there were complaints of initial burning, but no irritation effect was observed.

Cleanser "B" was used in a series of 34 patients with otitis externa as a cleansing agent without water. No irri-

tation was noted in these patients. It was not possible to tell whether this cleanser had any therapeutic or preventive value.

In impetigo and sycosis barbae of the face, cleanser "B" was used as a shaving cream. It was not possible to determine whether there was any therapeutic value, since it was used alone in only a small series. As a shampoo for the scalp, it was not acceptable, because of its residual effect.

In seborrheic dermatitis of the scalp, it was not as efficient as shampoos containing selenium sulfide.

In general, waterless cleansers of the cream type are of value in clinical dermatology. This would include use in acne, removal of tenacious soils in patients with dermatitis of the hands, cleansing routines in the prevention of diaper dermatitis, external otitis, and removal of sticky ointments. As in industrial dermatology, these materials cannot always replace the conventional cleansers.

Itching

Itching is the awareness of local cutaneous discomfort that evokes an almost irresistible scratch reflex. It is perhaps the commonest dermatological complaint.

Recent investigations support the concept that itch is closely related to cutaneous pain; it results from low intensity stimulation of the free endings of the nerve fibers that subserve pain. Itch cannot be induced in skin denuded of its epidermal layer.

Many authors believe that there are two types of itch and pain. The first is a superficial, sharply localized, pricking itch that corresponds to the pricking or "fast" pain of short duration following the stimulus. The second type is a diffuse, poorly localized burning itch that persists for some time following the stimulus. It corresponds to burning, radiating, "slow" pain.

Recently, the existence of two components of pain has been questioned by Margaret H. Jones who believes that the slow component is an artifact. If this is true of pain, it is true of itch also.

Pain will cancel itching anywhere in its dermatome immediately and for some time after the pain has subsided. Thus scratching erases unpleasant weak itch impulses by superimposing stronger more tolerable pain impulses.

It has also been noted that for a considerable distance surrounding the site of a painful stimulus the skin becomes hypersensitive to itch stimuli—an area of "itchy skin" that itches intensely when lightly stroked or rubbed. A similar zone of itchy skin surrounds the site of an intense itch stimulus. Thus, although scratching temporarily alleviates itching, the ensuing pain may be ringed by a still broader zone of itchy skin subject to additional scratching with subsequent reinforcement and prolongation of itching.

Various stimuli provoke the peripheral sensory receptors to itching. Common pruritogenic irritations are contact with prickly animal or vegetable fibers (hair and woolens) exposure to certain chemicals (soaps, drugs, insect stings, plant poisons), temperature changes, air drafts, and slight pressure changes. Endogenous irritants such as retained sweat (prickly heat) may cause inflammation with intolerable itching. In fact, itching is characteristic of most of the inflammatory dermatoses including the hypersensitivity types (urticaria). Intractable itching is also a common and conspicuous symptom of certain systemic diseases such as diabetes, and liver disease.

W. B. Shelley and his associates have shed light on the mechanism of itching as a result of interesting studies with itch powder or cowhage. Further investigation revealed that all proteinases in the endopeptidase group and active at normal pH were capable of giving rise to an excruciating itch sensation within a few moments after injecting an incredibly small amount intraepidermally. Significantly and in contrast with other pruritogenic chemical agents, the itching occurred without detectable cutaneous changes.

From these data these workers postulated that proteinase activity is commonly responsible for mediating the itch sensation. Any stimulus of the epidermis that induces itching forces release of cellular proteinase (cathepsins). Likewise, systemic conditions that are accompanied by itching set the stage for physiologic liberation and activation of microscopic amounts of circulating proteinase (plasmin). Itching without evidence of inflammatory changes of the skin is relatively common and is a diagnostic clue in some neurogenic and psychogenic disorders, arteriosclerosis, anemias, intestinal parasites, and tuberculosis.

The itch threshold has been observed to fluctuate with the patient's psychic status. This influence is reflected in the fact that itching is generally less severe in the morning before fatigue has developed than in the evening.

The relief of itching is not always simple.

Theoretically the most efficacious local measures are those designed to protect the peripheral nerve endings from pruritogenic stimuli or to reduce their reactivity to the stimuli. These measures should avoid increasing vasodilation, heat, and tissue anoxia which tend to intensify itching. Simply cooling the area, removing pressure, applying protective dressings, or elimination of contact with allergens, chemical, and physical irritants often provides relief.

The use of topical anesthetics is apt to be futile except on excoriated skin, because absorption through intact skin and even some injured skin is insufficient to anesthetize the sensory nerve endings. Some of these preparations complicate matters by their irritating and sensitizing properties. A few of the newer local anesthetic ointments, however, are reported to give improved results. Topical antihistaminics often fail for lack of sufficient absorption.

Topical preparations containing corticosteroids are used extensively as antipruritics by dermatologists. Apparently in the stubborn dermatoses most favorably affected by the corticosteroids, relief of inflammation cuts through the vicious itch-scratch-itch spiral. The steroids, particularly hydrocortisone combined with topical antibiotics to combat secondary infection, have firmly established their superiority and popularity in the management of many otherwise resistant cases.

In addition to local therapy, systemic medication may prove worthwhile. Systemically administered drugs possessing peripheral action on pruritus include cortisone, ACTH, antihistaminics and procaine. The vasoconstrictor action of epinephrine has been utilized to good advantage, as has the anhidrotic action of such drugs as atropine.

Sometimes it is desirable to depress itch perception with centrally active drugs. Salicylates are among the most effective of these drugs. Although morphine and other narcotics relieve pain, paradoxically they tend to intensify itching. Some clinicians have found that tranquilizers have a salutary effect in severely involved cases that require long-term reduction of central perception of the itch sensation. —*Scope* 5:16, 1957.

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Perfumer's Shelf

Solidified Flavor Composition

A solid flavoring composition and its method of preparation are described in U.S. Patent 2,809,895, issued October 15, 1957 to H. E. Swisher and assigned to Sunkist Growers, Inc.

This invention relates to a solid essential oil containing composition suitable for use as an ingredient of foods, pharmaceuticals, perfumes, soaps, cosmetics and other products. More particularly, the invention is concerned with a method for forming a finely dispersed essential oil-corn syrup emulsion which is solidified and further treated to give an essential oil product in solid form and protected from oxidation.

The objects of the invention are to preserve the natural flavor of the essential oils and especially the cold pressed oils; to permit their extended storage without deterioration; to produce an essential oil composition suitable for direct use in the preparation of food products; to produce a solidified water soluble essential oil composition from which the oil is readily available and which has every characteristic of freshly extracted cold pressed oil, and to obviate the chemical taste and odor associated with essential oils which have been weighted with brominated oils.

Basically the process consists in emulsifying, at a temperature of between about 85° C. and 125° C., an essential oil, to which an antioxidant and a dispersing agent have been added, in a corn syrup solids solution having a moisture content of between 3 per cent and 8½ per cent; forming a solid emulsion from the hot fluid emulsion by extruding into pellet form, or by agitating in a hot immiscible liquid, cooling rapidly to cause solidification of the emulsion globules and separating from the cooled immiscible liquid, or by cooling to solidification, and grinding; washing the resulting particles with an essential oil solvent and drying them by vacuum removal of solvent to produce a free flowing relatively non-hygroscopic granular material. This end product is an essential oil dispersion consisting of amorphous particles of corn syrup solids which form a matrix for the essential oil and protect it from contact with oxygen and moisture.

Prior to its addition to the hot corn syrup solids solution, it is critical that the essential oil be treated with minor amounts of 4-methyl-2,6-ditertiary butyl phenol, butylated hydroxyanisole, or some other oil soluble, heat stable antioxidant, since the heat of the molten corn syrup will very rapidly cause the degeneration of some of the constituents of the essential oil into undesirable terpene compounds in the absence of such antioxidant treatment.

In addition, a minor amount of a dispersing agent is added to the essential oil or with it, since, without a dispersant, the essential oil and corn syrup will not form the required finely dispersed emulsion, but will form a poor emulsion consisting of relatively few large individual droplets of essential oil within the corn syrup.

The following representative emulsifiers are suitable for use; diacetyl tartaric acid ester of a mono-diglyceride, monoglyceride sodium sulfo-acetate, polymeric alkylaryl polyether alcohol, polyethylene glycol fatty acid esters, sodium lauryl sulfate, glyceryl monostearate, acetylated monoglycerides, citrus stearoptene, lecithin, gum arabic, locust bean gum, guar gum, tragacanth gum, pectin, pectin albedo, agar and algin.

Hydroxycitronellal Process

U.S. Patent 2,812,355 was issued November 5, 1957 to A. L. Fox and assigned to Colgate-Palmolive Company for a new process of preparing hydroxycitronellal. One of the more common ways of preparing hydroxycitronellal is by a procedure which involves the formation of a bisulfite addition compound of citronellal, effecting hydration at the double bond of the citronellal portion of the addition compound, as in the presence of sulfuric acid, and treating the bisulfite addition compound of hydroxycitronellal to remove the bisulfite and thus liberate the free hydroxycitronellal.

The synthesis of hydroxycitronellal by the foregoing method is a difficult one, and is generally productive of the desired compound only in poor over-all yields, due to erratic results and low yields obtained from the hydration step. In a series of eight experiments employing these prior methods, or only minor variants, the average yield from the hydration step itself was only about 37 per cent, the individual results ranging from a low of 10 per cent to a high of 71 per cent.

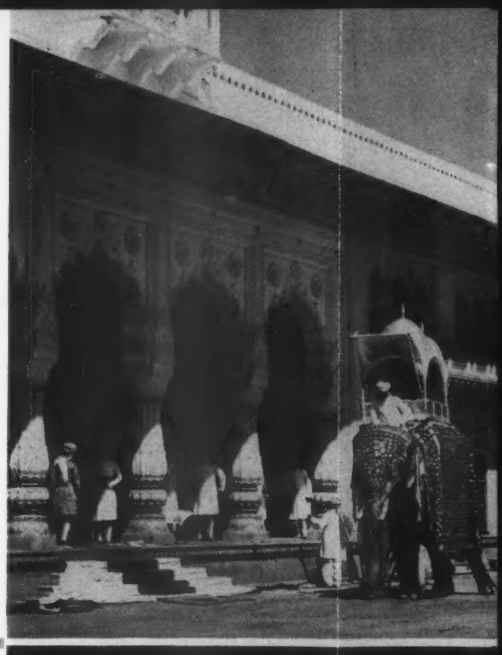
One of the principal objects of the present invention is to provide a new and improved process for the production of hydroxycitronellal by a method which will permit substantially improved yields in a reproducible manner. A further object of the present invention is to provide a new and improved method of hydration of the citronellal-bisulfite adduct to the hydroxycitronellal-bisulfite adduct in a manner which will permit the ultimate recovery of the desired hydroxycitronellal with reproducible yields of the order of 65 per cent or more of theoretical.

According to the present invention, the hydration step is carried out in the presence of liquid sulfur dioxide, while the bisulfite adduct is dispersed in a suitable organic solvent for hydroxycitronellal such as toluene. Any solvent may be employed so long as it is inert and water-immiscible, its purpose being to extract the hydroxycitronellal from the aqueous hydration reaction medium containing sulfuric acid. Benzene, toluene and xylene are additional examples of suitable solvents for the purpose.

Technical citronellal (82 per cent citronellal) is reacted with sodium bisulfite in the form of a 30 per cent aqueous solution at room temperature, thereby resulting in a citronellal-bisulfite adduct of 87 per cent purity. The initial techni-

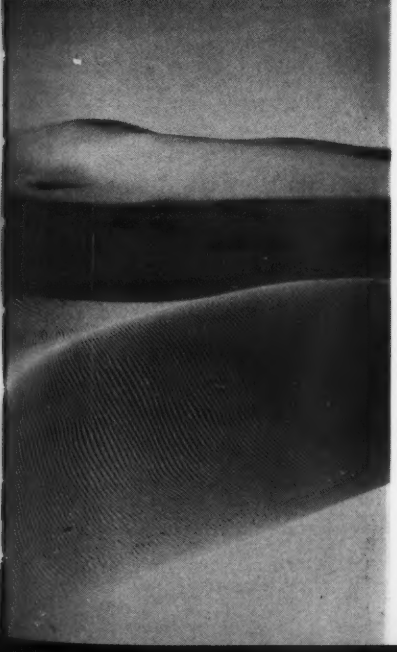
Tender Touch

This sweetly-scented composition has life, lift and exhilarating freshness. Its fragrance is distinctly floral—a brilliant bouquet modified with citrus and deftly accented with aldehydes. A warm, woody note lends interesting contrast, and suitable fixation assures uniformity of its original character at all stages of evaporation.



COUNTERPOINT

In this composition our perfumers have used a warm, woody effect with an unusual combination of spices to complement a bright, brilliant motif of rose, lilac and jasmine. A beautifully balanced, harmonious effect is the result. Delightful topnote; excellent fixation; moderately priced for perfumes, toilet waters and colognes.



SAMUM

An original and exotically beautiful fragrance—gentle and caressing, but potentially irresistible. It is warm and spicy with a balsamy, resinous odor complex and an underlying floral modification composed of carnation, orange flowers, jasmine and rose. In perfumes and toilet waters, its fragrance suggests elegance and refinement.

sindhu

A soft-scented, alluring and exotic fragrance composed of tropical woods, gums and balsams, enhanced in beauty by the use of selected florals discreetly blended. Recommended for a luxury line of extracts, toilet waters and face powders.

HIGH WIRE

A breathtaking, beautifully balanced formulation for extracts, toilet waters, colognes, lotions and powders. This perfume is an attractive floral complex with warm, woody modification of its base. A faint suggestion of citrus-aldehyde gives it a pleasantly refreshing, somewhat heady topnote, while appropriate fixatives complete a formulation that is well rounded and enduring.

GIGOLETTE

Spirited and vivacious, this fragrance has the airy freshness of a French cologne. Here is a light floral bouquet with citrus-aldehyde topnote, nicely complemented by fullness and body from a faintly spiced, woody base. Recommended for economy in producing attractive, low concentration perfumes and toilet waters.

A PORTFOLIO of PERFUMES . . . . .

Here, briefly described, are six more outstanding fragrances offered for the consideration of discriminating perfumers. From this varied selection you may find just the type desired for your new line of extracts, toiletries and cosmetics. We invite your serious consideration of these exclusive offerings.

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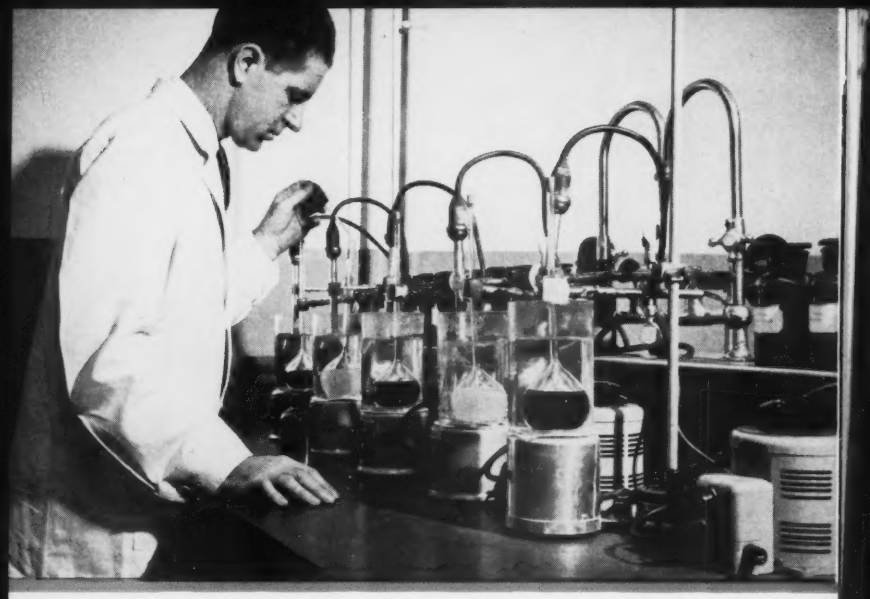

Test for Determination of Ketones in an Essential Oil.

Continuous improvement in the laboratory techniques employed in our quality control operations tends toward the goal of speedier and more accurate results. Even in so small a matter as *manual* vs. *mechanical* agitation of liquids—as in the test for determination of ketones in an essential oil, shown above—we use a magnetic stirrer which keeps the reaction under constant automatic agitation. Note, also, that a water bath surrounds each of the oil-containing flasks and that thus, by a simple system of emersion, heat can be *uniformly applied* at all points, to the materials under examination. It is true that, in itself, each is but a small detail. Nevertheless, if there is one thing experience teaches, it is that only through conscientious attention to such details can product perfection ever be reached. And that, of course, is FRITZSCHE'S ultimate goal.

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OH, NO! NOT THAT TONIC!

SINCE our little friend so pointedly rejects *"that"* tonic, it seems a fair assumption he has in mind some other medicine which is *not* objectionable. Truth is, he has. The big difference is this latter has a flavor much more appealing to his tender, sensitive taste. As a result of this, it is even more effective because patients take it *willingly* without complaint and *regularly* as prescribed. . . . Today, the proper flavoring of medicinal products is a highly specialized and very important field of endeavor, and we are rather proud that our Pharmaceutical Flavor Laboratory has had a pioneering and leading role in its advancement. On the strength of this rich experience, we should like to offer you its unlimited facilities for the study of flavor improvements that might well increase the acceptability of your medicinal product. Such work would be in strictest confidence and without cost or obligation until and unless we satisfied you.

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cal citronellal may be first purified by distillation and the adduct-forming reaction may be carried out in the presence of an inert water-miscible solvent such as methanol for convenience in handling the reaction mixture.

The citronellal-bisulfite adduct is separated, dried and ground to a white powder. One hundred grams of the dry, ground adduct are suspended in 200 ml. of toluene and the mixture cooled to —10° C. 200 ml. of liquid sulfur dioxide are then added to the reaction mixture and the mixture placed in a reaction vessel fitted with a Dry-Ice reflux condenser. Two hundred ml. of 50 percent sulfuric acid are then added to the reaction mixture with stirring. Agitation of the reaction mixture is continued for five hours while holding the temperature between 0° and —10° C. At the end of this time the sulfur dioxide is removed under slightly reduced pressure, the temperature not being allowed to rise above 0° C., and the mixture is then neutralized with solid sodium carbonate. 70 ml. of a 36 per cent formaldehyde solution in water are added to regenerate the hydroxycitronellal from its bisulfite addition compound, and the mixture is stirred for three hours. The layers are separated and the aqueous phase is extracted with four 100-ml. portions of toluene. The toluene extracts are combined and the toluene is then removed by distillation. The residual material is vacuum-distilled and 45.6 grams of hydroxycitronellal are obtained, representing a yield of 69 per cent of theoretical. The hydroxycitronellal is in highly purified form and is eminently suited for use as a perfume ingredient.

Synthetic Ambergis Odors

U.S. Patent 2,809,996 was issued October 15, 1957 to Max Stoll and assigned to Firmenich & Co. for compounds having an ambergris odor, and their preparation.

It is still completely unknown what the fragrant components of ambergris are. Its principal constituent, the triterpenic alcohol ambrein, is scentless in the pure state and yields by degradation a single fragrant product, namely dihydro-γ ionone which does not truly smell like ambergris, and several other, scentless, products.

It is, on the other hand, known that sclareol, the diterpenic glycol, which is the principal constituent of the essential oil from clary sage, is always accompanied by a faint scent of ambergris although it is scentless in the pure state. The ozonolysis of one of its neutral degradation products, namely the anhydride of the 1-butylone-2-hydroxy-2,5,-5,9 - tetramethyl - decaline which is also called sclareol oxide followed by a hydrolysis or by a reduction of the ozonide formed, yields a mixture of at least four products, all of which are scentless in the pure state, viz.:

(1) 2 - acetoxy - 2,5,5,9 - tetramethyl-decalyl - acetic acid (Formula II);

(2) A mono - acetylated γ-glycol, namely the 2 - acetoxy - 2,5,5,9 - tetramethyl-decalyl-ethylol (Formula III);

(3) An acetylated hydroxy-aldehyde, namely the 2 - acetoxy - 2,5,5,9 - tetramethyl - decalyl - ethanal (Formula IV);

(4) A neutral product of unknown constitution of the empirical formula $C_{18}H_{30}O_2$.

The unexpected discovery has now been made that by transforming either the acid of the Formula II, or the glycol of the Formula III, or the aldehyde of the Formula IV, by the loss of acetic acid, into an unsaturated aldehyde, a product is obtained, namely the $\Delta^{1,2}$-2,5,5,9-tetramethyl octalyl acetic aldehyde, which has a powerful and clinging ambergris scent. It has also been ascertained that the corresponding alcohol, the $\Delta^{1,2}$-2,5,5,9-tetramethyl octalyl-ethanol possesses a strongly clinging scent of an ambergris character. These two unsaturated substances, which have never before been synthetically produced, may advantageously replace the unknown fragrant substances of the ambergris. They form new and valuable compounds which can be used in the perfumery and cosmetics trade wherever a scent of an ambergris character is desired.

It has further been ascertained that the isomers, the double bond of which is placed between the carbon atom 2 and one of its adjacent carbon atoms (apart from carbon atom 1), present likewise a scent of an ambergris character. Thus, in a general manner, the unsaturated compounds presenting a 2,5,5,9-tetramethyl-octalyl group or a 5,5,9-trimethyl-2-methylene-decalyl group, all having a double bond at the carbon atom 2 and presenting an aldehydic- or alcoholic radical in the side chain attached to the carbon atom 1, have been found to be new scent products of interest for perfumery.

Musc 781

Woody and slightly fruity overtones distinguish this new aromatic and lend it individuality. In addition to its impressive fixative properties, the presence of Musc 781 in perfumes at very low concentrations makes itself felt at all stages of evaporation. This property is particularly evident in alcoholic solutions where it produces a mellowing effect on the alcohol.

A descriptive booklet and samples are available from Polak & Schwarz Inc., 667 Washington Street, New York 14, N. Y.

Scentovision

Scentovision, a blend of motion pictures and appropriate odors, was patented recently.

The inventor is Hans Laube, a Swiss. His associates refer to him as an expert in osmology, the science of odors.

The patent (2,813,452) explains that after a motion picture is made it is to be cued for odor signals. The exhibitor is to receive, along with the can of film, a battery containing the set of perfumes.

A working model was set up two years ago in the balcony of the Cinerama-Warner Theatre, with pipes to carry the perfume under the seats. A ten-minute pilot film, with seventeen scenes and seventeen odors, was shown experimentally to a private audience.

Backers of Scentovision hope to interest theatres in permanent installations when they get a full-length film.

Mr. Laube's most recent experiments have been with supermarket displays. Slides of various products are accompanied by such odors as orange, lemon, goulash, cheese, banana, smoked ham and chocolate pie. The inventor also sees a future for synchronized perfume emissions from television sets.

The trouble with earlier efforts to please both the nose and the eye, according to Mr. Laube, was that one smell remained when the reason for it had passed. Commrecial perfumes contain fixatives, whose purpose is to make them last longer. He removes the fixatives, to make his scents temporary. If they don't disappear quickly enough, he sprays the room with a neutralizer, and follows this with the next perfume.

The various scents used, such as wood, cocoa, rose, peach, honey and violet are stored in a "battery of cells." As the machine picks up a signal, it dips a nozzle into one of the cells and pumps out the perfume, or neutralizer.

The Scentovision Corporation of which Len Ruskin is president, has offices at 15 West Forty-fourth Street. The Stanley Warner Corporation, owners of Cinerama, financed development of the invention. The patent is owned by Mr. Laube and Bert S. Good of New York.

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PRODUCT	TYPE	USES	ADVANTAGES
Stepanol WA (Paste)	Sodium lauryl sulfate	Liquid or paste creme shampoos. Emulsifier for use in cosmetics.	Outstanding foam and foam stability. Light stable color • bland odor. Superior detergency and wetting.
Stepanol WAQ (Heavy Liquid)	Sodium lauryl sulfate	Same as above, but for use where viscous liquid instead of paste is desired.	Same as above.
Stepanol WA Special (Low Viscosity Liquid)	Sodium lauryl sulfate	Liquid creme shampoos.	Same as above plus very low inorganic salt content.
Stepanol WAT (Clear Fluid Liquid)	Triethanolamine lauryl sulfate	Clear liquid shampoos. Foaming hand cleaners.	Low cloud point, outstanding color, foaming, detergency and wetting.
Stepanol WAT-S (Clear Fluid Liquid)	Triethanolamine salt of higher fatty alcohol sulfate	Clear liquid shampoos.	Same as above plus superior emulsification. Slightly darker and heavier than WAT.
Stepanol ME Dry (Dry White Powder)	High active sodium lauryl sulfate (U.S.P.)	Liquid and dry shampoos. Emulsifying agent for waxes and creams, dentifrices.	Excellent foaming, detergent and emulsifying properties. Soluble in water.
Stepanol AM (Heavy Liquid)	Ammonium lauryl sulfate	Liquid, creme or paste shampoos.	For use where low ph is required. Good detergency, wetting and foaming.
Stepanol MG (Light Amber Liquid)	Magnesium lauryl sulfate	Same as above.	Same as above, but gives better cloud point than sodium or ammonium salts.
T6-A (Light Amber Viscous Liquid)	Alkanolamide	Liquid bubble bath.	Excellent foam stabilizer in presence of soap.
T6-B (Light Amber Viscous Liquid)	Alkanolamide	Clear and creme shampoos.	Thickening agent. Auxiliary detergent, some emolliency.
LIPA (Light Ivory Color Flake)	Alkylolamide	Detergent hand cleaners. Creme shampoos.	100% active. Superb foam stabilizer. Auxiliary detergent. Nonionic in character.

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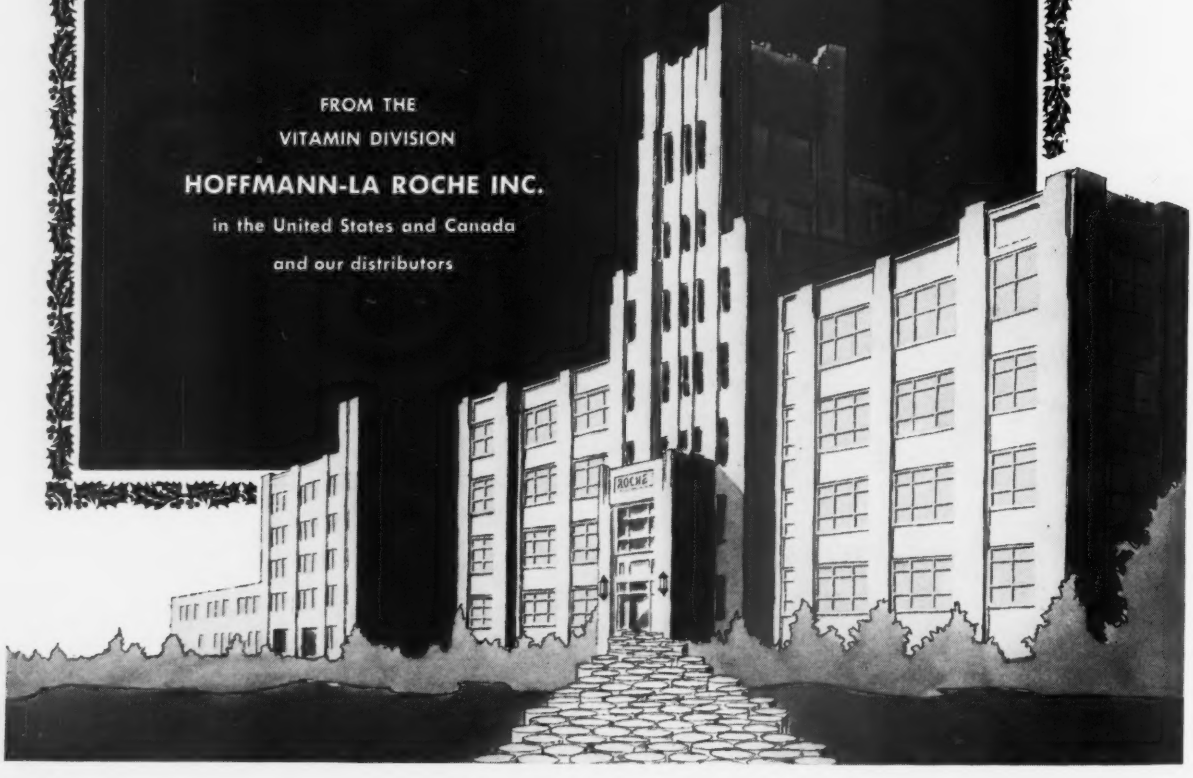

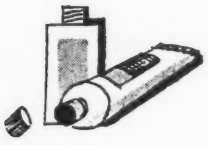

Advancing Therapy

Chlorothiazide Conference

The New York Academy of Sciences, section of Biology, and Merck Sharp & Dohme Research Laboratories jointly sponsored a conference November 8, 1957 on "Chlorothiazide and other Diuretic Agents."

As background for the consideration of the action and use of diuretics it would be desirable according to *R. W. Berliner*, to present a systematic picture of the mechanisms involved in renal electrolyte transport and the individual metabolic processes underlying them. However, virtually nothing is known of these and the accidental discovery of diuretic activity has contributed more to identification of processes involved in transport than has knowledge of transport processes to the rational development of diuretics.

Diuretic activity can be defined for present purposes as the capacity to produce significant net loss of strong electrolyte. While theoretically it is possible that diuretics could be effective by increasing the rate of glomerular filtration, the only diuretic activity of significant value so far encountered has been attributable to depression of renal electrolyte transport.

In exploring the sulfonamide-type of compounds, *J. M. Sprague* found an unexpected high order of activity among the aromatic disulfonamides, particularly benzene-1,3-disulfonamides and their derivatives. Furthermore, many of these compounds show qualitative differences from the recognized carbonic anhydrase inhibitors in that they produce a marked increase in chloride ion excretion, as well as sodium ion excretion. Further substitution in the benzene ring alters activity markedly. The halogens augment activity; 4,5-dichlorobenzene-1,3-disulfonamide has a particularly favorable activity. Amino and acylamino groups also have a marked enhancing effect. In the acylamino series (acetylamino, butyrylamino, hexanoylamino, benzoylamino), activity increases as the aliphatic acyl group is lengthened. When the acylamino group occupies a position ortho to a sulfamyl group, ring closure may occur with the elimination of water to yield a benzothiadiazine-1, 1-dioxide. These compounds are of particular interest since they exhibit activities of both the carbonic anhydrase inhibitor and the organic mercurial-type of diuretic agents. They are effective orally and parenterally and promote the excretion of both sodium and chloride ions in approximately stoichiometric quantities. Substitution in the benzenoid ring enhances activity; halogen in the 6-position is highly effective. 6-Chloro-7-sulfamyl-1,2,4-bensothiadiazine -1, 1-dioxide (chlorothiazide) shows outstanding activity. An alkyl group, or an hydroxyl at the 3-position, also results in active compounds.

Xanthine diuretics were briefly reviewed by *G. H. Mudge and I. M. Weiner*. Mercurials were considered in greater detail with discussion of the following topics: primary and secondary effects on tubular electrolyte transport, segmental localization of site of action, succinic dehydrogenase inhibition, metabolic fate and excretory products of organic mercurials, nature of potentiation by acidosis, activity of organic *vs* inorganic mercurials with detailed reference to acid stability. The hypothesis that is most consistent with the total available data is that organic mercurials act by the local release of mercuric ions within the renal tubule.

It is widely accepted according to *A. Gilman* that the renal regulation of acid-base metabolism depends primarily on the secretion of hydrogen ion by the renal tubular cells. This process presumably involves exchange with monovalent cation in the tubular urine, primarily sodium ion. As a result of this exchange, bicarbonate ion is removed from tubular urine, the urinary buffers are acidified and the diffusion of ammonia into tubular urine is facilitated. Carbonic anhydrase is essential for this process to provide carbonic acid, either as a direct source of hydrogen ion or as a buffer to prevent a rise of intracellular pH. Inhibition of the enzyme reduces the rate of hydrogen ion transport.

In the course of study relating the structure of organic compounds to their effect on electrolyte excretion an unusual heterocyclic compound (chlorothiazide, Diuril) was found by *K. H. Beyer* to increase substantially the renal elimination of sodium and chloride by the dog. F. C. Novello and J. M. Sprague have identified this compound as 6-chloro-7-sulfamyl-1, 2, 4-benzothiadiazine-1, 1-dioxide.

Chlorothiazide is unique, pharmacologically, in that it has the structure of a carbonic anhydrase inhibitor and an enhancing effect on salt and (secondarily) water excretion resembling that of a potent organomercurial diuretic agent. Whereas most carbonic anhydrase inhibitors cause an increased excretion of sodium and bicarbonate ions, considerable potassium and essentially no increase in chloride excretion, chlorothiazide causes a more or less equivalent excretion of sodium and chloride ions with little increase in potassium and bicarbonate elimination, ordinarily. Most carbonic anhydrase inhibitors cause an increase in urinary pH and a metabolic acidosis that results in the development of refractoriness to the agent, whereas chlorothiazide may cause no change, an increase or a decrease in urinary pH and no metabolic acidosis and has a continued effectiveness during daily administration for protracted periods of time. The sulfamyl group with which this antienzymic effect is associated is critical to the utility of chlorothiazide, for if the the group is blocked by alkylation or substitution the resultant compound is inactive.

Whereas organomercurial diuretic agents have a slow onset by any prac-

tical route of administration and more or less erratic oral activity, chlorothiazide is promptly and essentially equally active in dogs whether administered orally or intravenously. The affinity of mercurials for sulfhydryl groups is somehow critical for their diuretic efficacy, in which respect they differ from chlorothiazide. Chlorothiazide is active under experimental conditions of NH_4Cl acidosis or $NaHCO_3$ alkalosis. The compound has a very low order of toxicity when administered acutely (mouse I.V. LD_{50}—1120 mg./kg) or chronically.

The distribution of the compound in the body appears to be limited essentially to extracellular fluid, except in the kidney where it is secreted by the tubules in addition to being ultrafiltered to the extent of 30 to 50 per cent at the glomeruli. In addition to its rapid renal elimination, chlorothiazide has been found to be excreted by way of the biliary system.

The rational approach to the problem of congestive heart failure according to *R. Ford* includes the exhibition of agents to increase cardiac output (digitalis), decrease venous presure (ganglionic blocking agents and rest), and decrease the abnormal bodily retention of sodium (natriuretic or "diuretic" agents). Since all of these agents produce diuresis, they may all be considered "diuretic" agents. Observations of urinary sodium excretion and serum electrolytes illustrate that certain diuretics are repetitively effective (mercurials, chlorothiazide, and chlorazinil) while others present a problem of drug tolerance (aminouracils and carbonic anhydrase inhibitors) demanding an interrupted dosage schedule. Serum electrolyte changes indicate the tendency toward hypochloremic alkalosis with mercurials and chlorothiazide which may require attention. The carbonic anhydrase inhibitors are occasionally productive of systemic acidosis or hypokalemia which may limit their usefulness.

The choice of a diuretic agent in congestive heart failure may depend on several factors: The need for daily administration, underlying renal decompensation which may prohibit an agent producing acidosis, the feasibility of oral or parenteral routes of administration, and, finally, the potency of the diuretic. Utilizing bioassay techniques, the comparative potency of various diuretics following single doses and selecting meralluride (Mercuhydrin) as "one" (1.0) may be established. Diglucomethoxane (Mersoben) is 1.3 (I.M.), chlorothiazide is 0.8 (oral), aminometradine (Mictine) is 0.7 (oral), chlorazinil is 0.5 (oral), chlormerodrin (Neohydrin) is 0.5 (oral) and acetazolamide (Diamox) is 0.25 (oral).

Over one hundred patients with edema have been given chlorothiazide therapy by *J. Laragh*. Controlled metabolic data have been collected on 32 hospital patients. The group consists largely of patients with congestive heart failure. Nine patients with cirrhosis of the liver and persistent ascites have been treated with chlorothiazide on the metabolism ward. The results from this group were given in detail and compared with the effect of chlorothiazide in heart disease, chronic lung disease and nephrosis. The effect of chlorothiazide on acid-base balance, uric acid and aldosterone excretion has also been studied, and plasma levels of chlorothiazide have been measured.

Diuretic therapy is considered by *G. Schreiner* in 4 major renal situations: 1) where edema is the prominent problem and renal insufficiency is absent, e.g. nephrotic syndrome, hyper-aldosteronism, etc; 2) salt retention with moderate renal insufficiency, e.g. acute, subacute and chronic glomerulonephritis, renal lupus, Kimmelstiel-Wilson's disease, preeclampsia and pyelonephritis; 3) moderate to severe renal insufficiency in an attempt to induce an osmotic diuresis and 4) special situations such as the management of polycystic disease or uric acid nephritis. The edema of cirrhosis and congestive heart failure may coexist or complicate any primary renal disease.

Chlorothiazide has been found to be a potent, safe and effective adjunct in the treatment of a wide variety of renal disorders except in patients with a marked reduction in glomerular filtration rate.

In acute experiments in normal subjects according to *R. I. S. Bayliss* the predominant action of chlorothiazide is to increase the urinary excretion of sodium and chloride, an effect similar to mercurial diuretics. Also, in some cases, there is less significant increase in potassium and bicarbonate excretion—resembling carbonic anhydrase inhibition. In longer term studies in edematous patients, sodium and chloride are eliminated in approximately equimolar quantities, and the serum bicarbonate level remains constant. No instance of hypochloremic alkalosis has been encountered. Potassium loss is increased by hypokalemia and is a problem only in chronically-ill patients on rigid sodium restriction receiving continuous chlorothiazide treatment.

In normal subjects 1 gram chlorothiazide by mouth is as potent as 2cc. of mersalyl by injection. Furthermore, in edematous subjects, chlorothiazide is often successful when mercurial diuretics are inactive.

Treating Hypercholesterolemia

Phenylethylacetic acid or its amide was administered by M. F. Oliver and G. S. Boyd (*The Lancet*, p. 829, 1957) orally in various dosages from 1.2 to 5 g. daily to 24 hypercholesterolemic men with coronary disease. In 1 man, who received 4 g. of phenylethylacetic amide daily, there was significant depression of the plasma-cholesterol level and the lipoprotein ratios. In most of the remaining men there was no significant action of phenylethylacetic acid or its amide on the circulating lipids and lipoproteins. Of the 6 men who received 5 g. of phenylethylacetic acid daily 4 showed slight lowering of the plasma-cholesterol level (less than 12 per cent in each case), but there was no change in their lipoprotein ratios; all of these 4 men experienced nausea or vomiting and could not take their customary diet.

These results suggest that phenylethylacetic acid lowers the plasma cholesterol level in only a small proportion of people; and most of these developed anorexia, nausea, or vomiting. These findings are quantitatively at variance with the observations of Cottet and Mathivat (1955), who recorded lowering of the plasma-cholesterol in 75-80 per cent of patients receiving phenylethylacetic acid in doses of 2.4 to 3.2 g. daily. On the other hand they support the reports of Frederickson and Steinberg (1957) and Grande et al. (1957), who did not observe any significant influence of phenylethylacetic acid or its amide on the circulating lipids and lipoproteins.

Linodoxine Capsules (Pfizer) are red soft gelatin capsules containing 500 mg. linoleic acid (as safflower oil), 1.4 mg. pyridoxine hydrochloride, 7.12 mg. mixed tocopherols, and 0.009 per cent propyl gallate antioxidant. The preparation is intended to provide essential unsaturated fatty acids to the diet and to reduce elevated serum cholesterol levels and is available in bottles of 100 and 250.

Floropryl (Merck, Sharp & Dohme) is now available as an ophthalmic ointment containing 0.025 per cent of diisopropyl fluorophosphate for the treatment of certain types of glaucoma and strabismus. Tubes contain 3.5 grams of the ointment.

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Samples and technical data are available upon request.

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(*Continued from page 804*)

keep the crew in space suits throughout its tour of duty, but this would not be feasible for long stints such as manning a satellite or making a Martian run. Another, employed in Major David G. Simon's 32-hour balloon flight to 100,000 feet in August, is to replace the nitrogen in the vessel's atmosphere with helium, which does not dissolve in the blood so readily; in theory men steeped in such an atmosphere could stand decompression long enough to have at least a chance of slapping a patch over the offending puncture. One unexpected rule runs contrary to all previous human experience: in a situation of explosive decompression, the spaceman must *not* hold his breath, despite his natural instinct to do so. His lungs will survive far better if he lets the air rush out of them.

Far better, however, not to sustain a puncture at all than to have to cope with one after it has happened. Just how likely is such an accident?

At present we can only guess, but the recent satellite shoots will provide hard figures. Sputnik I's change-over from beeping to a continuous tone after five days aloft probably reflects the Russian satellite's first puncture, letting out the nitrogen with which the satellite was filled and actuating a diaphragm switch.* The fact that the radio continued to broadcast data thereafter indicates that the hit was a micro-meteor—a fast dust particle—which simply vaporized as it hit, leaving behind a pin-hole in the satellite's hull but not otherwise damaging the vehicle. No really damaging hit was sustained during the three-week life of Sputnik I's batteries.

This is a good record for so thin-skinned an object, and furthermore it provides a gratifying match for the calculations of Dr. Fred L. Whipple, one of the key men on Project Vanguard. Whipple had previously estimated that a micro-puncture could be expected about once every five days, and a heavier hit about once a month. Presumably major, disabling hits could largely be avoided by timing flights in between major meteor showers, most of whose orbits are well known. Sputnik I was launched, doubtless for reasons having nothing to do with research, just in time to encounter autumn's most important meteor swarm, the Orionids; in a manned vehicle such a coincidence would not be advisable.*

What role the pharmaceutical industry will be able to play in the solution of these problems is not known now, of course, but there are some obvious areas of research which might lead to extensive participation in the adventure. Existing motion sickness drugs will doubtless prove useful, and it is possible that other types of disorientation might be smoothed out by ataraxics or drugs related to them. Research into drugs which may help the body to resist ionizing radiation is already under way (with an eye to a considerably grimmer end use); these, too, would be invaluable, although there is serious doubt that any pharmacological approach will be successful against heavy primary cosmics. Considerations of weight of cargo alone are likely to insure that space medicine kits will lean heavily on the broad spectrum antibiotics; infectious disease in the confines of a space vessel would obviously be a death-warrant for all concerned.

This summary of the medical problems confronting future space travellers makes the space frontier sound formidable indeed—which to be sure it is. But in the United States, such experts as the Astronautics Panel of the American Rocket Society (Dr. Haber, Robert Bush, John DeNike, Homer E. Newell Jr., and Milton Rosen) have been viewing the firing of a 1000-pound payload into an orbit as a project for the International Geophysical Year 1982-83; whereas the USSR has already orbited a heavier load in *this* IGY, just last month. Obviously a major breakthrough has been made, and from now on we may expect the age of space flight to burgeon as rapidly in the second half of the 20th Century as flight in the atmosphere mushroomed in the first half.

The problems are new and exceedingly difficult; but all the same, we are on our way.

*At present this is simply a guess, but there is general agreement on this interpretation. The actual situation is known only to the Russians at this writing.

YLANG-YLANG

(*Continued from page 743*)

in Zanzibar, North of the Comoro islands, and also saw the oil being distilled in a pilot plant at the Clove Growers Association in Malindi, Zanzibar, I would not dare forecast for Zanzibar a great future as a supplier of ylang-ylang oil. But this oil might become a running "by-product," or "off-season product" from the modern stills in Malindi where, however, the clove stem oil remains the product of paramount interest. The annual production of ylang-ylang oil in Nossi-Be was at the time of my visit estimated at 18 to 20 tons, while the Comoro Archipelago have already surpassed the 20-ton mark. Smaller quantities are produced in the Sambirane district in Madagascar opposite Nossi-Be, where other French perfume houses since long have produced the oil. Reunion produced in 1955 a total of 1200 kilos of ylang-ylang oil in the two remaining distilleries.

Surprisingly enough, the greater part of all ylang-ylang oil is still produced in primitive native installations. About 35 to 45 per cent are distilled in French installations of rather modern type. Such installations can produce relatively more of the so-called "Extra" or "First" qualities of the oil, than the so-called direct-fire type native stills. A peculiar detail by the native stills is, that the steam is produced in boilers which are heated by mangrove wood, from the so-called "paletuviers," the only wild-growing trees found in abundance in the island, since these trees are no more exploited for tanning purposes. The bark and wood from these trees contain a high percentage of tannin

(*Continued on page 827*)

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Antiseptics, Disinfectants, Fungicides, and Chemical and Physical Sterilization, *Edited by George F. Reddish, Ph.D., St. Louis College of Pharmacy, 2nd Ed., 975 pages, Illus., Lea & Febiger, Phila., (1957), cloth,* **$15.**

Pertinent information relative to antiseptics, disinfectants and fungicides, as well as chemical and physical methods of sterilization, is set down and evaluated in this book. It represents the combined efforts of 28 authorities who cover important facts relating to antimicrobic agents generally, exclusive of antibiotics and chemotherapeutic drugs. Iodine, the mercurials, alcohols and other antiseptics are discussed first, followed by disinfectants and fungistats and fungicides. This edition contains three new chapters: Sterility Tests and Methods of Assuring Sterility, Methods of Testing Sanitizers and Bacteristatic Substances, and Ultraviolet Radiation as a Germicidal Agent.

Pharmaceutical Calculations, *by Bradley, Gustafson, and Stoklosa, Third Ed., 325 pp., Lea & Febiger, Phil., (1957), cloth,* **$4.50.**

This textbook is concerned exclusively with the arithmetic of today's applied pharmacy. Almost every problem represents actual pharmaceutical experience, constantly suggesting the atmosphere of the laboratory or dispensing room. With this text, students calculate only with quantities that they will later deal with in their professional work. Stress is put upon the importance of keeping track of significant figures and allowable percentage of error when using numbers representing measurement of weight or volume. Drugs and Chemicals referred to are familiar in present-day practice.

The Chemistry Of Organic Medicinal Products, *by Jenkins, Hartung, Hamlin, Jr., and Data, Fourth Ed., 569 pp., John Wiley & Sons, Inc., New York (1957), cloth,* **$10.75.**

This new edition shows an extensive revision of the material in Jenkins and Hartung's third edition, thus bringing the subject matter well up to date. New material contained in the revised work includes: chapter on antibiotics—increased section on hormones—all references, where possible, to the in vivo action of drugs—introduction of new compounds of pharmaceutical interest.

British National Formulary 1957, *pocket size, cloth, The Pharmaceutical Press, London, 226 pp.,* **Price 6s. 6d. (postage 5d.)**

This fourth ed. of the National Formulary is now published under the new title of the British National Formulary, by authority of The British Medical Association and The Pharmaceutical Society of Great Britain. It is a handbook of convenient size for desk or pocket and contains a comprehensive range of preparations and formulae sufficient to meet the needs of prescribers in hospital and general practice, and of pharmacies. New preparations have been added. The section on Poisoning has been extended and a note on drugs of addiction has also been added. The Notes for Prescribers have been thoroughly revised and a paragraph on cortisone, hydrocortisone and allied substances has been included in the section on Hormones.

Pure Food and Drugs in California, *by August F. Glaive, formerly Chief, California State Food and Drug Laboratory, 204 pp., The National Press, Palo Alto, (1957), cloth,* **$4.50.**

The author here sketches the background, European as well as American, of this vital field. He relates the growth in power and influence of the California State Board of Health and the development, from very modest beginnings, of the State Food and Drug Laboratory to its present important role. He also tells about the more colorful cases and legal battles in maintaining fair standards and reasonable protection for the public.

A Concise Guide to Plastics, *by Herbert R. Simonds, Consulting Engineer, 318 pp., Illus., Reinhold Publishing Corp., New York, (1957), cloth,* **$6.95.**

This book describes all known American commercial plastics, including those still in the laboratory stage. It instructs in the selection, use and forms of plastics, and contains discussions of which ones best suit particular products. The information includes basic data on strength, properties, processes, production and prices. An important feature lists the 43 most important plastics producers with their addresses, the names of chief officers, company organization and background, products, trade names, and descriptions of operations.

The Dermatologist's Handbook, *by Ashton L. Welsh, M.S., M.D., Assistant Professor of Dermatology and Syphilology, University of Cincinnati, 427 pp., 9" x 11", Charles C. Thomas, Publisher, Springfield, Ill., (1957), cloth,* **$15.**

The purpose of this work is to organize into a rational systematic classification, with the object of instruction and ready reference, that large number of topical and internal therapeutic agents concerning which a dermatologist must have knowledge. The author has sought to present and arrange the diverse subject matter in this book in a manner which will afford better understanding of, and a desk-top reference to, essentially all of the agents about which a modern dermatologist must be informed. This large work is divided into three main parts: Topical Therapy – Internal Therapy – Reference Data.

New Unguent Bases and Loons, *by Isaac Kenneth Hoffman, Research Staff, U.C.L.A., School of Medicine, Division of Dermatology, 152 pp., Chemical Publishing Co., Inc., New York, (1957), cloth,* **$4.75.**

Seven chapters including the introductory one, cover washable oil-in-water unguent bases, washable oil-in-water lotions, nonwashable water-in-oil unguent bases, nonwashable water-in-oil lotions, washable anhydrous oil-in-water unguent bases and nonwashable anhydrous water-in-oil unguent bases. The author is familiar with the standard raw materials available for cosmetic as well as ointment formulation and has given over 250 formulas, with directions for compounding (and a name for each). The book should serve as a valuable reference work whenever cosmetic or pharmaceutical formulation is contemplated.

C.S.M.A. Aerosol Guide, *looseleaf, 89 pages, Chemical Specialties Manufacturers Association, Inc., New York,* **$8.**

This guide is an assembly of recommendations and developments of the Committees of the Aerosol Division of the Chemical Specialties Manufacturers Association, Inc. All the recommendations are the result of long and careful study by the committees of all phases of the industry and by consultations with many authorities in regard to transportation, legal and other matters. Vendors of aerosol packages should study these recommendations and insist that they aer carefully followed and fillers of pressurized packages should make certain that basic recommendations are followed.

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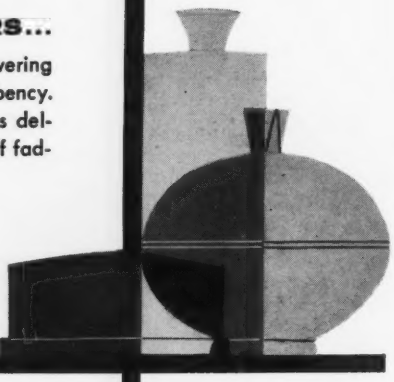

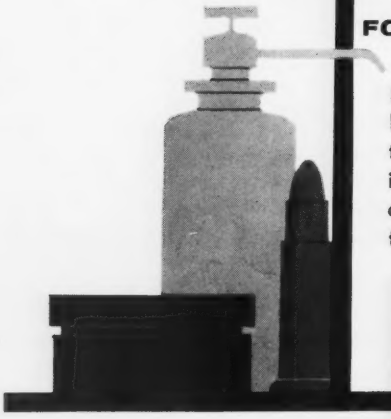

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Reader's Questions . . .

Egg Shampoo: *We have formulas for a number of good shampoos and are successfully marketing one at the present time. As an additional product, rather than as a replacement, we wish to produce an egg shampoo and would appreciate your comments, especially as regards label requirements.* CHICAGO.

According to Keithler, egg has emollient action and can be added to the shampoo as whole egg or as the dried egg powder, the latter preferably being reconstituted before use. More important is a recent letter to the Toilet Goods Association from the Bureau of Enforcement of the Food & Drug Administration conerning the labelling of egg shampoos. An egg shampoo should contain one egg or the equivalent in dried egg in the amount of shampoo required for one shampooing of the hair. When a smaller proportion of egg is present in the shampoo, the preparation should not be labelled "egg shampoo" but may be described as shampoo with egg. The word egg should not have the same prominence as the name of the product and the amount of egg ingredient should be mentioned on the label. Where the amount of egg present is less than two per cent, the proportion is considered to be insignificant and "egg" should not be mentioned in the labelling.

Face Powder: *We inclose a copy of our face powder formula and hope you can assist us in improving it. When first applied to the face (with or without a foundation) it seems to be very good but the color soon darkens and becomes yellowish. Would the "bleeding" of colors in the presence of moisture be responsible for this color change?* NEWARK.

The color change you mention is sometimes ascribed to "bleeding," but I think this is wrong. When pigments, earth colors or lakes, are moistened with water, and more especially with oils, the color becomes darker and yellower. If, however, an opacifier or covering agent is present, this will not take place or occur to only a limited extent. Your formula contains only about 3 per cent of zinc oxide and covering power will be enormously improved if the zinc oxide is increased to 10 or 15 per cent. The pigments now present will have to be increased and perhaps the whole shade will have to be rematched with the standard because of the whitening agent.

(*Continued from page 824*)

and related chemicals. The smoke from this wood will, in certain cases, give a phenolic-catecholic by-odor in the ylang-ylang oil distilled in such primitive stills.

During the latest years there has been an increasing demand for a so-called "complete" oil, which is the total distillate from an uninterrupted distillation. This could be a result from increasing difficulties in saturating the demand for an "Extra" quality, which very often has lured certain wholesale houses into compounding a "First" quality with the aid of synthetic perfumery materials to obtain the wanted "Extra" notes. A genuine "Extra" ylang-ylang oil is actually a very rare merchandise to-day. It is also doubtful, whether the commercially available "total" oils are truly *total*, uninterrupted distillates. Neither my own observations nor the recent reports from Dr. Ernest Guenther point in that direction. To the contrary, the distillation is still carried out as a fractionated one, and on demand of a "complete" oil, the fractions are mixed in the proportions, in which they are or have been produced. Theoretically, this should result in a fairly true, "complete" oil. But the method is not satisfactory to the customers.

At this point, I should perhaps turn the reader's attention to the almost forgotten perfume oil, called "cananga oil." This oil is still produced in modest quantities in Java and elsewhere in Indonesia from the flowers of the same tree as ylang-ylang oil is distilled from. Java cananga oil is a "complete" oil, but differs significantly from any one of the ylang-ylang oils in regard to olfactory properties. Partly because of the fact that cananga oil is distilled from crushed (and perhaps slightly decayed) flower material, the entirely different method of distillation, and because of the haphazardly chosen flower material for cananga oil, there is only a chemical similarity between this oil and the ylang-ylang oils. Cananga oil is, thanks to its very high content of (odorless) highboiling materials, a very good fixative, and thus lends itself for use in soaps, where ylang-ylang would be too expensive in relation to its effect in most cases.

Apart from the distilled oils, also extraction products of the flowers of ylang-ylang are made on the very habitat of the tree. I had the opportunity of visiting the SPPM (Societe des Plantes a Parfums a Madagascar) extraction plant in Nossi-Be. In the Comoro Archipelago, the extractions are carried out by the large French company Bambao, whose installations are of comparatively recent date. They have also experimentally produced other flower extraction products. It is a pleasant surprise for a perfumer to find such modern installation in these remote habitats of the natural raw material, although of course, it is necessary to have at hand extraction plants if a concrete or an absolute is to be produced. But it is equally encouraging to observe, that the industry of perfumery raw materials seems to avoid no effort in order to constantly produce new and interesting raw materials, against which the synthetic perfumery materials will

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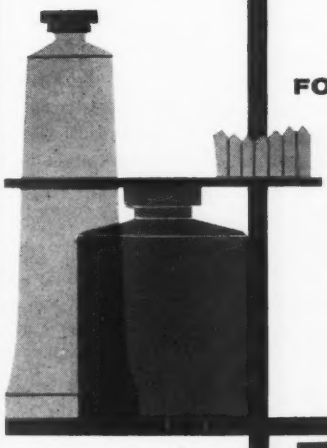

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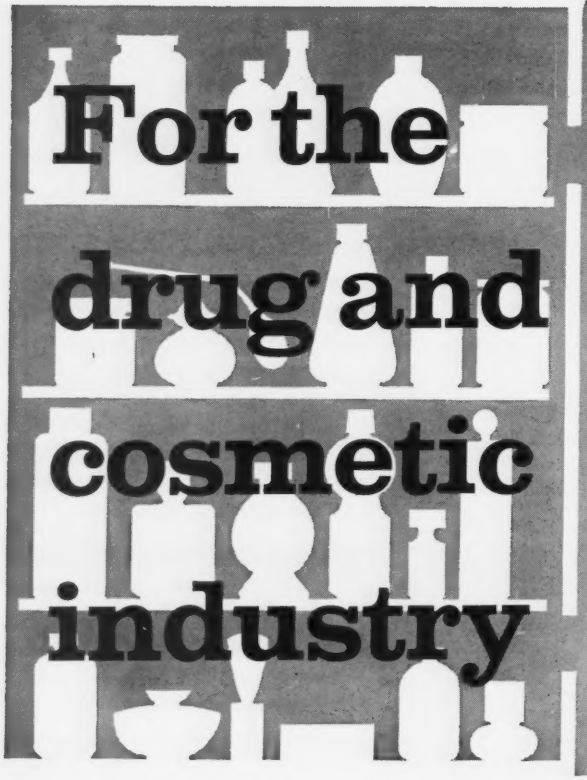
find a hard time of competing. I feel thoroughly convinced that, although the essential oils may suffer a considerable loss through the steadily increasing industry of synthetic perfumery raw materials, the natural raw materials will retain their advantage: that absolutes, concretes, resinoids, etc. will remain extremely difficult to duplicate synthetically at a competitive price. In this fact is rooted much of the future for the natural raw materials in their fight against the synthetics.

It is furthermore always reassuring that as much work as possible is carried out on the habitat where, 1) the cost of labor is the lowest, 2) either no remedies for "cutting" the oils are at hand or 3) where the producers have no interest whatsoever of "cutting" or "playing around" with the merchandise. After all, we must admit, that certain European and American factories and suppliers of perfumery raw materials often handle these precious oils, absolutes, concretes etc. with much less veneration for mother nature's products than we could wish, and it is not always the customer's or the competition's fault, that these tendencies arise.

As far as ylang-ylang is concerned, we must add, that a correctly produced absolute of ylang-ylang flowers can be classified among the very finest perfumery raw materials at our disposal. As it furthermore belongs to the less expensive absolutes of the "flower" type of odor, one dare foresay for this product a solid future. No "Extra" or "Extra superior" ylang-ylang oil can replace an absolute of ylang-ylang—and vice versa. But, as mentioned, the "Extra" ylang-ylang is no more produced in the quantity in which it used to be, and the term "Extra" has also changed along with the development of the distillation technique. SPPM in Nossi-Be maintains a minimum specific gravity of 0.970 at 15° C. for "Extra" oils, while the Comoro "Extra" oils are usually slightly higher, occasionally beyond 1.000.

The plantations of ylang-ylang trees in Nossi-Be are, however, now becoming too old, and a replanting will be necessary if this island wants to keep up with the competition from the Comoro Archipelago, where the plantations are still young. Here the cyclones have caused considerable damage during the last decades, particularly the 1953 cyclone which destroyed valuable property and cost over 100 lives. Almost all the older ylang-ylang trees in these islands were wiped out or heavily damaged during this disaster, but the Comoros are under rocket-like development, and a few export figures will reveal that these small islands (four islands totalling 850 square miles) really can produce considerable quantities of these valuable natural raw materials. During 1954, the islands exported 114 tons of cured vanilla fruits ("pods") worth 500 million Francs (1954 Francs!) and 44 tons of essential oils, worth 300 million Francs. The production of vanilla, it can be seen from these figures, is now almost



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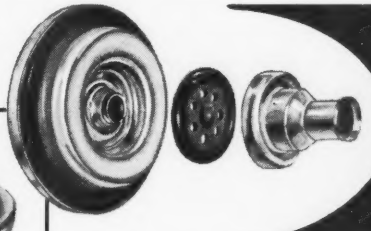
3 times as big as that of the old favorite "Bourbon," from the island of Reunion, although the quality of the latter vanilla brand remains superior. Another peculiar fact is, that vanilla and essential oils amount to about 80 per cent of the total export value from the Comoros. Of the above mentioned 44 tons of essential oils, lemongrass counted for nearly 25 tons, while ylang-ylang amounted to almost the balance, close to 19 tons; 1955 was over 20 tons. Only very small amounts of other essential oils are produced in the Comoros, such as basil, neroli and petitgrain bigarade.

Similar conditions are ruling the economy of Nossi-Be, which is a true "Perfume Island." I spent a whole week in that wonderful little spot, and took part in all the work and leisure distractions of the French inhabitants there (less than 100 Frenchmen live in Nossi-Be). Among the most romantic and picturesque off-time distractions were the excursions to the still smaller neighbouring island of Nossi-Komba, which means: "The Island of Monkeys." A strange variety of the monkey-fox like maki live here in peace and sociability. They are extremely friendly and curious, and will gladly eat from your hand. While the Frenchmen were skindiving, picnicking or practising with bow and arrow, I went afoot to the interior of this almost circular, 4-mile diameter, volcanic jungle island. I was most surprised to find it almost covered with plantations of ylang-ylang, a little coffee, and a very old culture of huge mango trees. During such expeditions through the jungle, one could really come into contact with nature. It is through such excursions, that one can achieve a thorough knowledge of, what wonders mother nature can produce. Apart from the man-introduced ylang-ylang trees, I found here giant spiders, butterflies of up to 8 or 10 inches of wingspread, chameleons, snakes, lizards and crabs. But I could enjoy all these wonders at ease, for Magadascar and its islands do not shelter one single dangerous animal: No wild beasts, no venimous snakes, no poisonous insects. Only two hazards exist: The malaria-bearing mosquito, and the shark. But with the SAP (anti-paludism control) on one side, and the wonderful, modern swimming pools at all larger beaches on the other hand, even these two hazards are eliminated.

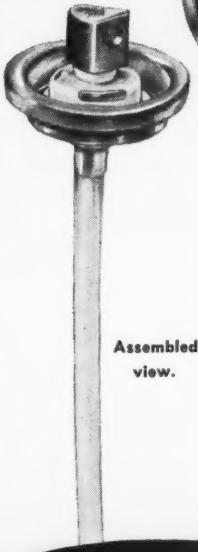
There are a few, two or three, distilleries for ylang-ylang oil on the tiny island of Nossi-Komba. Just sufficient to treat the locally produced flowers. As far as I could detect, only a couple of Frenchmen lived here, but if they happened to like mangoes, they would certainly not starve (during the two seasons!). I literally waded in mango fruits during my foot trip through the dense jungle. The ylang distilleries were all of the direct-fire type.

It is, however, worthwhile remembering, that a correct distillation from a choice flower material, even in a primitive apparatus, will yield a better oil, than a careless distillation in modern installations, or a distillation from a haphazardly chosen material. When

Exploded view of OEL Aerosol Valve.



Positive operation ... no clogging with the OEL AEROSOL VALVE



Assembled view.

Simplicity is the keynote of the OEL Aerosol Valve. It has only three parts (see exploded view)—the nearest approach to integral construction of any aerosol valve. The unique rubber diaphragm insures accurate sealing, freedom from clogging, and positive action.

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3. Uniform flow rates due to "above-the-valve" control.
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the flowers are picked, they should immediately be brought to the stills, and if they cannot be treated at once, they should be spread on a dry concrete floor in deep shade, and, if possible, cool. The details of the cultivation of the trees and of the process of distillation have been described fully and comprehensively in the recent work of Dr. Guenther ("The Essential Oils," vol.V., pages 279-304) but I would like to draw the attention to a few very important factors:

The flowers must be picked at the proper stage of maturity, and distilled (or extracted) within a few hours. The total process of distillation is, however, often more than 24 hours. The "Extra" and "Extra Superior" fractions will distil within the first hour of treatment. The yield of these fractions is very small, only a fraction of one per cent of the flower material, and the economy of the production of ylang-ylang oil is based upon the sale of *all* the fractions. It is more the handwork of picking flowers, than the tedious and time-requiring work of distilling, that brings up the price of the end-product. In this fact lies much of the advantage of the extraction products. The yields are good, although very different according as benzene or petroleum ether is used as solvent, and the concrete in turn yields even up to 80 per cent of absolute. This is why the ylang-ylang concrete is more or less liquid, a fact that has puzzled many consumers. Now, a liquid ylang-ylang concrete does not necessarily mean a genuine one, but a solid concrete of ylang-ylang should arouse the customer's suspicion. The absolute (from concrete) of ylang-ylang represents a high concentration of the top notes of this flower, one of the finest perfumery raw materials among those produced on a larger scale.

In Nossi-Be I was guided all over the island by the director of SPPM or his associate, and I also had a visit to their extraction plant, constructed amidst the dense plantation of ylang-ylang trees. These are typical in their "crippled" appearance. In their country of origin (Philippines etc.), these trees are left to natural growth, but some smart persons found out that if they cut off the crown (the vertical top branches) of the trees at the age of 4 to 7 years, which means a height of 12 to 16 feet, the trees would not grow higher, but only send out lateral branches, conveniently located for the hand picking of the flowers without the use of ladders or, as in the Philippines, long bamboo sticks. No doubt, the "crippled" trees withstand the cyclones much better than would a 50 or 100 feet high slender tree (which is the natural height of the ylang-ylang tree).

The extraction plant was constructed in suitable distance from the distillation halls, because of fire hazard and explosion danger from the solvents in use. It is quite a problem to control the evaporation of petroleum ether, when the temperature is around 85° or 95° F. all year round. For the same reason, I could not take any indoor photographs of the extraction plant. My flash would be too risky to use. But as the

extractions could not adapt themselves to normal working hours—the flowers must be treated right after being harvested—the extraction plant was illuminated from outside searchlights. The electricity was produced locally in gasoline-driven generators.

On our way back from one of these tours in 4-wheel driven Land-Rovers (English Jeeps), we picked up some lots of ylang-ylang oil from other French distillers, associated to the larger French export houses. Occasionally, ylang-ylang oil is shipped by air to Europe, but Nossi-Be has the fourth largest harbor in Madagascar, and is visited quite often by large ocean-freighters, which anchor up off-coast. The Comoro islands usually send their oil by air to Nossi-Be or Madagascar for faster shipment to the European or American customers, but even these small islands are visited fortnightly by French cargo ships.

With much regret I, too, had to be shipped off Nossi-Be soon. My further itinerary through East Africa had to be kept on the tight schedule as outlined years in advance. With the faithful car aboard, I embarked a French cargo-steamer bound for Mombasa on Christmas eve to say "Veloma" or "see you again" not only to the hospitable Gomes' from SPPM, but also to this scented island, shrouded in a heavy perfume of ylang-ylang, the "Flower of Flowers."

PAN-AMERICAN PHARMACY

(*Continued from page 744*)

dustry from our various countries—to give thoughtful consideration to how the technical advances may best benefit human health."

Dr. A. H. Holland Jr., of the Food and Drug Administration, told the Congress:

"Section 801 (d) of the Federal law in effect is an exemption from the requirements of our Federal law so that the manufacturer may meet the requirements of your laws and the specifications of the purchaser. While some argue to the contrary, the United States Congress has not seen fit to decide what is good for you or what specifications and standards you should employ. To do so, of course, would be presumptuous. This is the prerogative of your own respective governments. This does not mean, however, that we in the Food and Drug Administration, and many others too, believe that we should not make every reasonable effort to help you obtain the same fine medications that are available here. The vast majority of United States manufacturers follow good practices in both their domestic and export operations. The business leaders in the drug community will appreciate both the intrinsic and material value of their good name. They have built their business and their firms and prospered because they were wise enough to perceive the folly of fraudulence and the fraternity of fair dealing.

"Back in the late 40's and early 50's there was a series of hearings before committees of the United States Congress to explore the advisability of revising

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the export provisions of our Federal drug law. The Food and Drug Administration is on record as favoring those legislative changes which will promote truthfulness, good products and fair dealing. We still wish to be so counted, for it's our duty to attempt to improve the performance standards throughout industry. The leaders in drug research and drug manufacturing will always be far ahead. In a sense, this is part of the reward and is to be expected. It is part of our job to see that the laggards in the field adopt and employ standards of good practice and new and improved methods as they become available . . .

"Lest you believe I am speaking only of problems and practices of your countries and not those of my own, let me assure you that we approach imports on the same philosophical and legal basis. Regardless of the research status or marketing status of a drug in other countries, if imported into the United States, it must meet and satisfy all of the requirements of our Federal law. The law is no harder or easier be the distributor a United States firm or some other national doing business in this country."

Dr. Ernest Volwiler, president of the American Drug Manufacturers Association and president of Abbott Laboratories, told the Congress that the U.S. patent laws play a vigorous role in sparking the development of new and improved drugs in this country. He continued:

"There are probably three fundamental reasons for the dramatic, worldwide forward march of medicinal chemistry during these past 30 years. One is that we have been able to define many therapeutic problems in chemical terms. The second is that we have developed means of measuring—both quantitatively and qualitatively—the activity of compounds in the human body. The third is that we can recognize more precisely what is needed. . . .

"Industrial production in the United States has trebled during the past quarter century. During this time we have drawn heavily on the basic scientific knowledge accumulated through the thought and research of the preceding century. It has often been pointed out, but it bears repeating, that we are using up our basic knowledge faster than we are replenishing it.

"The public has been fascinated and encouraged by the rapid progress of recent years in the development of valuable new drugs. Some of these have come from research workers in universities and clinics; others have originated in the research laboratories of drug manufacturing firms. Very few so far have had their origin in government laboratories. At the manufacturers' level, sales of the United States ethical pharmaceutical industry will probably be about $1.7 billion in 1957. A study recently completed indicates that industry research expenditures this year will amount to $127 million, as compared to $110 million in 1956. These outlays represent a high percentage of the drug industry's income, and the expenditures are expected to increase both in total amount and as percentage of sales. . . .

"The patent system has played an important role in the development of new and improved drugs. This is significantly true in the United States. Our system, which permits patenting of new compounds as well as methods of production, has sometimes been questioned; but in operation the system has greatly encouraged research and risk-taking, and it has strongly catalyzed initiative and research. Countries which do not have an enlightened and strong patent system are bound to impede progress and to suffer in the long run. . . .

"Many people have talked so much about $10 and $15 prescriptions that folks are surprised to learn that the average prescription costs only $2.74. Prescriptions costing $10 or more actually represent only one-half of one per cent of the total. This percentage, furthermore, has been declining. More than half of all prescriptions filled in the United States during 1956 were for less than $2."

PROPRIETARY MEDICINES IN N. Y.

(Continued from page 745)

the Pharmacy Act of New York State are adequate and sufficient."

The report states that under the Education Law, the New York State Pharmaceutical Association nominates candidates for appointment of the Board of Pharmacy by the Board of Regents, and says that "these nominations are tantamount to appointment." "This association is the trade association of retail pharmacists," continues the report. "It has sponsored and introduced legislation for a number of years to strengthen the retail druggist's monopoly in the sale of packaged medicines and opposed legislation that would have terminated this monopoly and permitted the sale of such proprietary medicines in stores other than drug stores."

"Section 6823, subsdivision 2, permits the Pharmacy Board to appoint a committee of pharmacists to try non-pharmacists for the sale of home remedies for alleged violation of Rule 17, promulgated by the board," says the report. "This is not a law passed by the Legislature that non-pharmacists are charged with violating—but a Pharmacy Board rule. The board has the authority to approve the findings of the Committee and to impose a penalty of up to $500 for each violation of its own rules.

"This subsection further provides that 'Neither the committee nor the board shall be bound by strict rules of procedure, or by the laws of evidence, in the conduct of these proceedings, but the determination shall be founded upon sufficient legal evidence to sustain it'."

Under this procedure, says the report, the Pharmacy Board:

1. Makes rules that have the force of laws.
2. Has the power to try a competitor and impose a penalty up to $500 for each violation of such rules.

3. Deny the right of trial by jury.
4. Deny the right of a fair and impartial trial before an unprejudiced tribunal.
5. Deny the common law right to a competitor to have his case heard in accordance with established legal procedure and in accordance with recognized rules of evidence.
6. The Pharmacy Board acts as investigator, prosecutor, judge and jury and sits in judgment of the acts of its competitors.

In addition, determination of the board is ". . . conclusive proof of such violation and penalty therefor."

"This procedure appears not unlike the 'kangaroo courts' in vogue in the Middle Ages which were outlawed by the Magna Carta and far distant from the enlightened legal procedure of the modern day," says the report.

"The Committee is convinced that the Board of Pharmacy should be deprived of the power to impose penalties upon persons other than licensed pharmacists and that subdivision 2 of section 6823 should be repealed forthwith.

"The repeal of this section would not leave the State powerless to protect the public against violations of the Pharmacy Act. Under subdivision 1 of section 6823 merchants who violate this act could be prosecuted in the criminal courts in the same manner as those who violate the medical practices act and violators of other professional codes. Misbranded or adulterated products may be seized under section 6815 and persons liable charged with a misdemeanor under section 6804 and injunctions may be obtained under section 6815 to prevent continuation of illegal acts.

"Power remains in the law for the Pharmacy Board to police the profession of pharmacy under section 6804 which permits the board to revoke or suspend licenses as well as to reprimand and censure licensed pharmacists guilty of illegal acts or unprofessional conduct."

"While the Committee is fully convinced that harmless proprietary medicines should be permitted to be sold by merchants in addition to licensed pharmacists, nevertheless it is believed that certain safeguards for the protection of the public should surround their sale," says the report. The Committee proposes a "proprietary medicine permit" be issued for a $5 registration fee paid to the Board of Pharmacy, and that the principal business of place be the sale of food or other merchandise for personal use or consumption. It would also be required that the owner be of good moral character, that he be over 21 years of age, that he be a citizen or shall have declared his intention to become one, and that he can read and write the English language.

Stating that "For several years the Pharmacy Board has been endeavoring to stop the sale of aspirin and milk of magnesia by general merchants, claiming these

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products to be listed in the U.S. Pharmacopoeia and hence not proprietary medicines," the report says: "We have all taken these products, practically since infancy and know that they are harmless if taken in accordance with label directions. In order to eliminate this Pharmacy Board claim it is recommended that these two products be added to schedule C of section of the Education law. All products in schedule C are permitted to be freely sold under subdivision 2c of section 6816 of this act."

The report concludes: "The amended bill of the Committee will remove the obvious inequities of the present law; it will restore the equality of justice that is the heritage of every American; it will properly and adequately safeguard the health of the consuming public. Public health has not suffered from the free sale of proprietary medicines in other states."

PASTEUR FERMENTATION CENTENNIAL

(*Continued from page 747*)

abandon. It is well known, for example, that his early studies on stereoisomerism not only opened this field of chemistry but also led to an appreciation of its significance in biology. What is less well recognized, however, is the intensity of imaginative thought that Pasteur devoted to the problem . . .

"While Pasteur's studies on the biological significance of stereoisomerism did not throw any light on the genesis of life, they have yielded a number of facts which had had far reaching influence on the development of biochemistry . . .

"Pasteur's highly imaginative and revolutionary views on the biochemical mechanisms of respiration and fermentation, and on their interrelationships, have been of far-reaching influence. He emphasized that living cells, whatever their own specializations and peculiarities, all derive the energy required for their living processes from the same general type of chemical reactions. This provided a basis for the doctrine of the biochemical unity of life, certainly one of the most important philosophical concepts of modern science . . .

"It was characteristic of Pasteur's scientific temperament that he never dissociated the theoretical aspects of science from their practical applications . . . Some of these applications like those having to do with the production of vinegar, wine, and beer, or with pasteurizing procedures, found their place in technology during his lifetime. The selection of healthy silkworms also became immediately an accepted practice in the production of silk. Living vaccines prepared from bacteria and viruses of attenuated virulence proved useful in Pasteur's own hands in the case of anthrax and rabies, and have continued to show their worth in the prevention of plague, tuberculosis, yellow fever, and other diseases of men and animals . . .

"It is in reference to the discovery of antimicrobial drugs that Pasteur's name has been mentioned most frequently during the past two decades . . . Pasteur never actually concerned himself with the development and use of drugs for the treatment of infectious diseases—probably because of his belief that prevention is better than cure . . .

"As is well known, he had developed his concepts of immunity from the study of vaccines made up of attenuated living cultures . . . Specifically, in the course of his work on rabies, he postulated that immunization might be due not to the living virus itself but to a nonliving substance which retained its immunizing power even after the virus had been killed by prolonged desiccation . . .

"All these observations and thoughts were gropings towards the knowledge of the chemical controls of immunity. The modern trend of utilizing, for immunization, substances separated from killed organisms, and amenable to purification and standardization by chemical procedures, would have satisfied his eagerness for well-defined methods . . .

"Pasteur had also the extraordinary idea of advocating the utilization of microbial life for the control of animal and plant parasites . . . Although the ultimate value of the method cannot yet be predicted, there is no doubt that Pasteur clearly visualized the potentialities and pioneered in the use of biological control through the activities of microorganisms.

"It can truly be said that his influence accelerated the exploitation of microorganisms for the benefit of man. Largely thanks to him, microbial life has now been domesticated, just as plant and animal life had been domesticated earlier in the course of civilization . . .

"It is generally assumed indeed that, in Pasteur's mind, mastery over microbial life required a direct action on the microbe. In reality, however, his writings clearly suggest another approach . . . He repeatedly expressed his conviction that the physiological state of the infected individual often decides the course of the infectious process. His scientific philosophy in this regard was extremely sophisticated, taking into account genetic and evolutionary concepts of adaptation . . .

"Pasteur did not hesitate to extend these views to the most important of human diseases. He accepted that resistance to tuberculosis was an expression of native hereditary endowment on the one hand, and that it was influenced on the other hand by the state of nutrition and by certain factors of the environment, including the climate. Even more boldly he suggested that the mental state of the patient did affect his resistance to microbial agents . . .

"Pasteur once formulated another hypothesis which, long regarded as naive, is acquiring new significance from recent studies on the effect of nutrition on infection. He had postulated that the immunity which often follows recovery from infection might be due to the fact that the body becomes depleted in some nutritional factor essential to the reproduction or activity of the parasite. . .

"Needless to say, Pasteur's 'exhaustion theory,' even though it applies to a few particular cases, ac-

counts for only a small part of the effects of nutrition and infection . . .

"It is only now that some of Pasteur's prophetic visions are acquiring significance for us, as we add new dimensions to the magnificent structure that he began to build. His writings should not be regarded merely as historical documents to be honored but left undisturbed in remote corners of library shelves; they carry a message that will encourage us as we try to reach beyond the conventional philosophies of fermentation and infection. His thought is still a living force reflected in many phases of contemporary biochemical, biological and medical sciences . . ."

The outlook for increased use of micro-organisms as producers of important chemicals and nutrients was discussed by *Dr. Marvin J. Johnson* of the department of biochemistry, University of Wisconsin. In a paper entitled "New Developments and Prospects in Fermentation Chemicals," Dr. Johnson remarked:

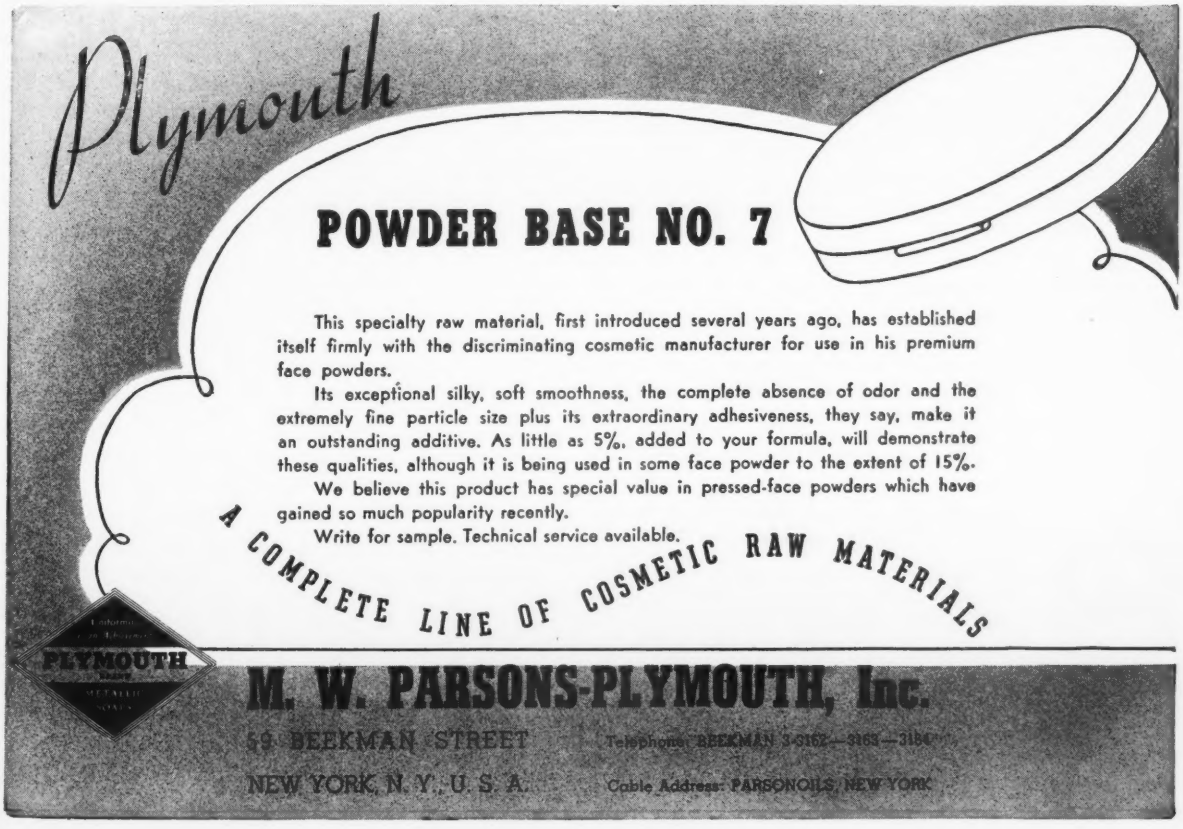
"The existence of the term "fermentation chemicals" implies that the chemist, instead of preparing a chemical compound himself, can enlist the aid of a microorganism. Microorganisms are skillful organic chemists, and they work long hours. Like their human brethren, however, they often exhibit an independence of spirit which makes them difficult to coerce . . .

"The alcoholic fermentation, of course, has been carried out on a large scale for millennia, and production of acetic acid from ethyl alcohol was also a traditional process. Commercial lactic acid production began before the turn of the century. Citric acid production began just before the first world war. The production of butanol and acetone began during the first world war, as did the fermentative production of glycerol. Large-scale gluconic acid production was reported in 1938.

"All of the fermentation products we have mentioned are products of the energy metabolism of the organism; end products of a normal or deranged carbohydrate metabolism. There exists, however, a large group of fermentation products that are not products of energy metabolism, but are compounds synthesized by the organism, and usually excreted by the organism. These are often complex in structure. Examples are riboflavin, polyglutamic acid, penicillin, and amylasse.

"The practical importance of this group of fermentation chemicals dates from the first commercial production of crude microbial riboflavin, in about 1937. About forty years elapsed between Louis Pasteur's discovery and the first commercial fermentation (other than the traditional fermentations). Another forty years elapsed before the first practical production of microbial secretion products. Today, the production of secretion products (largely antibiotics and vitamins) has become very important, and will undoubtedly increase in relative importance . . .

"In addition to products of energy metabolism, there is another product that is produced cheaply in large quantities from carbohydrate. Yeast cells, for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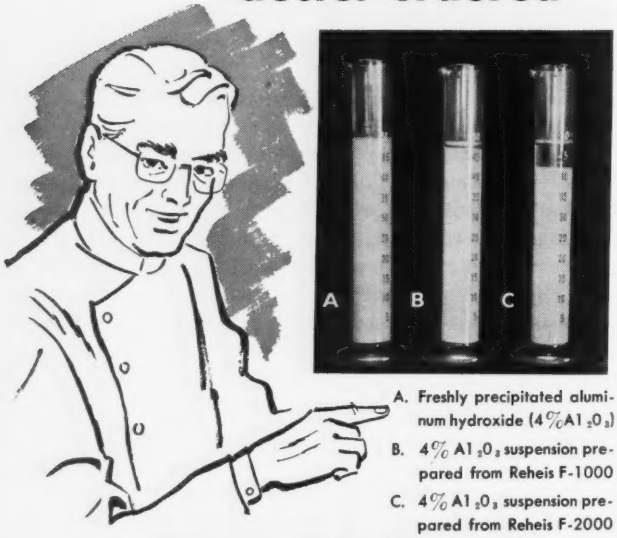

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use in baking and for use in animal feeds, are important fermentation products . . .

"For a long time, efforts have been made to introduce yeast as a human food in tropical countries. In the tropics, there is, in general, an abundance of carbohydrate, but a scarcity of protein, and large segments of the world population suffer from inadequate protein intake. Yeast, an excellent source of protein and vitamins, can be produced cheaply from carbohydrate and ammonia nitrogen. It has been impossible, however, to induce human beings to accept yeast as a major food item . . .

"Another group of fermentation products related to nutrition is amino acids. The amino acids methionine, lysine, tryptophan, threonine, and proline are often deficient in cheap plant proteins . . . Present research in a number of laboratories is being directed toward the production of essential amino acids by fermentation. In theory, it should be possible, by the judicious use of induced mutants, to produce almost any amino acid with the help of microorganisms. In practice, of course, many difficulties arise . . . It is certain that production of amino acids will be important in the future, and it will be interesting to see whether most of them will be made by fermentation or by synthesis.

"Among the compounds made in small amounts by microorganisms, the group that is at present of greatest importance is the antibiotics . . . But it is only if antibiotics can be found that are useful against some of our common virus infections that a great increase in antibiotic production for human therapy can be foreseen in the near future. Substances that are toxic to certain viruses but not toxic to animals have been shown to exist, but their rarity, and the difficulties involved in screening for antiviral antibiotics, have made progress slow. It is very difficult to predict the future of this field . . .

"The field of agricultural antibiotics is a new one. Much research is being devoted to the development of antibiotics active against plant diseases . . . An agricultural antibiotic or pesticide must be cheap, since large quantities must be used. The field appears promising, and interesting developments will probably occur within a few years.

"Antibiotics are widely used as animal feed supplements, mostly for poultry and hogs. It is not probable, however, that the use of antibiotics in this field will increase very greatly in the future . . .

A new field that has been productive in the past few years is the use of microorganisms to modify existing compounds. When a chemist wants to modify one specific site in a complex molecule (by oxidation, reduction, hydrolysis, or the like) he is usually in trouble. The specificity of enzymes, on the other hand, is well known. In many cases, it has been found possible to modify existing molecules with the help of microorganisms. An obvious example is the production of steroid hormones. An older example is the oxidation of sorbitol to sorbose, a step in ascorbic acid synthe-

sis . . . One can safely predict, that there will be further advances in this area. Recent work on the microbial conversion of indole to tryptophan is one example. Research in the field of microbial conversions is proceeding in many laboratories, and future developments should be rapid.

"For the past ten or fifteen years, there has been intense research activity in the field of production of new compounds by microorganisms. Some of the techniques developed deserve mention, because it is these techniques that have resulted in most of our advances, and it is these techniques, together with new, yet undiscovered techniques, that will make possible future advances. One group of techniques we may call screening techniques . . .

"Another technique that has been very useful in the creation and testing of induced mutants of microorganisms. The development of better screening procedures makes possible the testing of thousands of irradiated organisms, in a search for a mutant of desirable characteristics . . .

"Another possibility that I would like to mention is one that lies in the field of fermentation, but not in the field of microorganisms. Recent work on tissue culture indicates that it is possible to grow plant or animal cells under roughly the conditions used for large-scale growth of microorganisms. If the many problems involved can be solved, it will be possible to grow plant cells as one would grow microbial cells. Many valuable compounds now obtained from plants, alkaloids for example, may be obtained by plant tissue culture. The problems in animal tissue culture are greater, but the possibilities are also greater. Tissue culture is a field of great interest for the production of fermentation chemicals. Whether it will be a fruitful field remains to be seen."

The use of fermentation-produced antibiotic drugs in preventive medicine as well as in therapy, and in inhibition of the growth of tumors, was considered in "Trends in Antibiotic Research," a paper by *Dr. Paul R. Burkholder*, director of research of the Brooklyn Botanic Garden, and discoverer of the antibiotic chloramphenicol.

"The curious microbial antagonisms known to a few bacteriologists of the 19th century have grown into a virtual "antibiotic era" in the 20th century . . . The first phase of the science of antibiotics was concerned with the development of a concept, i.e., that living organisms produce chemical substances which are harmful to the life processes of other organisms, and that perhaps some of these substances might be useful in the prevention and cure of diseases. The second phase of antibiotics came through the chance observation of a prepared mind, ready to seize upon an accidental opportunity in order to develop antibiotics for clinical use. Alexander Fleming's memorable researches in 1929, and 1932, on the penicillin substance produced by the mold *Penicillium notatum*, set forth the facts concerning its powerful inhibitory prop-

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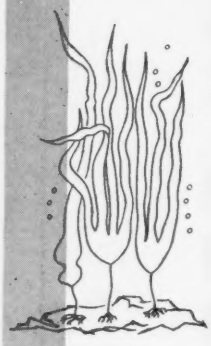

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erties against many common pathogenic bacteria and its lack of toxicity to animals, or human tissues. The third phase might be characterized by the appearance of broad spectrum substances which inhibit numerous kinds of microorganisms . . .

"Numerous narrow-and broad-spectrum antibiotics are continually being discovered in searches among bacteria, actinomycetes, fungi, algae, lichens, and higher plants. Some microorganisms produce many diverse kinds of antibiotic compounds, and it is also true that a given compound may be synthesized by different species . . . Numberous attempts are now being made to extend the spectrum of antibiotic inhibition to destroy neoplastic cells in the host. A fourth phase of research is now concerned with poly-antibiotic combinations of drugs for the purpose of levelling a "calculated crossfire" upon the etiological agents of disease . . .

"A somewhat different approach toward the achievement of antibiotic potentiation has come about through attention given to host reactions. It has been known for a long time that the patient actually has to get well by his own bodily defenses, whereas, therapeutic drugs may only lend assistance by arresting growth of the living agents causing the disease . . . The whole field is wide open for renewed studies on potentiation of the natural host reactions in disease. While antibiotics are used successfully to suppress germs in the body, too little attention has been given to helping the body toward lasting immunity.

"The important subject, mechanisms of action of antibiotics should, at least, be mentioned. Just as antiseptics act in various ways, by coagulating protoplasm of microbes, modifying their permeability or interfering with their enxyme reactions, so also do antibiotics show different mechanisms of interference in the life processes of susceptible microorganisms . . .

"An outstanding recent trend is found in the increasing manufacture of antibiotics for other than pharmaceutical uses. Important applications of antibiotics are being made for food preservation, as sprays to arrest diseases of fruit trees, vegetables, and flowers, as growth stimulants for pigs, poultry, mink and ruminants, and as agents to increase fecundity in cattle . . .

"Some of the current problems attendant upon the use of antibiotics in clinical medicine are concerned with allergy to drugs, toxicity of antibiotics, drug resistance of pathogenic microorganisms, and overgrowth of secondary pathogens, especially fungi. Attempts to overcome these difficulties are found in the use of new and better antibiotics, more effective combinations of good drugs, modified forms of drugs, different kinds of vehicles, adjuvants, and anti-allergens . . . The indiscriminate use of antibiotics, and inadequate dosages, can cause harm through hypersensitive reactions, blood dyscrasias, superinfections, and emergence of drug resistant persisters. The incidence of severe allergic reactions to certain antibiotics has

been somewhat disturbing . . . Most antibiotics should be regarded as potentially dangerous drugs in the hands of uninformed persons, and should be taken only on the advice of a competent physician.

"A great new era of preventive medicine lies just ahead, in which attention will be primarily devoted to means for potentiating long-lasting immunity against infections and arresting the course of degenerative and neoplastic diseases . . . Although therapeutic drugs lend assistance, the natural fitness of the body is decisive for survival . . .

"Along with chemotherapy and prophylaxis against invasions of microorganisms from without, there will be tremendous strides made in the future to provide mankind with proper birth control, adequate nutrition, and ways of preventing degeneration of body structure and function, and derangements of the mind. With increase of fundamental knowledge about diseases, man's sucseptibility to infections should come to be practically eliminated, and the normal vitality of youth greatly extended into old age. In the years ahead, as we now see it, there will be increasing need for therapeutic drugs, hormones, nutritive accessories, and potentiating chemicals to assist in regulating the natural fitness of our biological heritage. In the future conquest of disease and search for human happiness, man's greatest problem will not be pathogenic microbes; it will be himself."

A panel discussion of "Cellular and Biochemical Interplay Between Host and Parasite" was moderated by Dr. Dubos. Participants in the panel were Dr. Derrick Rowley of the Wright-Fleming Institute, London, Dr. W. Wilbur Ackermann, University of Michigan; Dr. L. J. Berry, Bryn Mawr College; and Dr. David E. Rogers, New York Hospital.

Dr. Johnson moderated the panel on "New Developments and Prospects in Fermentation Chemicals" with participants Dr. J. C. Sylvester, Abbott Laboratories, Chicago; Dr. A. F. Langlykke, Squibb Division, Olin Mathieson Chemical Co.; Dr. Frank H. Stodola, Northern Utilization Research and Development Division, U.S.D.A., Peoria, Ill.; and J. J. H. Hastings, Distillers (Biochemical) Ltd., London.

Important trends in antibiotic research were discussed by a panel moderated by Dr. Burkholder. The participants were: Dr. Milislav Demerec, Department of Genetics, Carnegie Institute of Washington; Dr. Hamao Umezawa, National Institute of Health of Japan, Tokyo; Dr. Arturo Curbelo, University of Havana; Dr. Jack L. Strominger, Washington University School of Medicine, St. Louis, Mo.; and Dr. G. F. Gause, Institute of Antibiotics, Academy of Medical Sciences, Moscow, USSR. Particular stress was placed upon the future of antibiotics as agents against tumors and virus diseases such as poliomyelitis.

Speakers at the dinner were John E. McKeen, President, Chas. Pfizer & Co., Inc., Dr. Vallery-Radot, Dr. Dubos and Herve Alphand, Ambassador of France.

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(*Continued from page 749*)

000 pounds in 1955; sales in 1956 totaled 100,000 pounds, valued at $465,000, against 90,000 pounds, valued at $525,000 in 1955.

The surface-active agents include synthetic organic detergents and wetting, dispersing, penetrating and emulsifying agents, not including finished soaps.

Originally developed as soap substitutes for the textile industry, surface-active agents have proved valuable in many other applications because of their varied and specific properties. Packaged household and industrial detergents account for about 75 per cent of the total output. Other applications are in the processing of textiles and leather, in ore flotation and oil-drilling operations and in the manufacture of paints, agricultural sprays, lubricants, cosmetics, foods and others.

In 1956, production of surface-active agents totaled 1,148 million pounds, or 11.4 per cent more than the 1,031 million pounds reported for the preceding year. Sales were 1,047 million pounds valued at $208 million, for a unit value of 20 cents, in 1956, compared with 962 million pounds valued at $229 million in 1955.

Sulfonated and sulfated alkylbenzenoid compound production reached 462 million pounds, sales were 441 million pounds valued at $70,396,000 or 16 cent unit value in 1956 compared with production of 449 million pounds and sales of 443 million pounds valued at $107,114,000, unit value 25 cents, in 1955. Although these detergents are of major importance in the formulating of shampoos, the bulk of the material is obviously used for household and industrial purposes. The listing for non-sulfonated nitrogen-containing cyclic surface-active agents includes quaternary ammonium compounds. Production in 1956 was 12,562,000 pounds and sales 8,591,000 pounds valued at $5,352,000. The group of acyclic non-cyclic nitrogen-containing surfactants includes amides and alkylolamides as well as some quaternary ammonium compounds. Production in 1956 was 69,745,000 pounds and sales were 65,160,000 pounds valued at $28,470,000. Sulfated and sulfonated acids alcohols and esters in 1956 were produced to the extent of 146,138,000 pounds with sales at 136,310,000 pounds valued at $30,573,000. These figures include data for the lauryl sulfates which are also reported separately. The 1956 production of sodium lauryl sulfate was 10,506,000 pounds, sales 9,049,000 valued at $4,879,000. Production of the triethanolamine salt was 3,095,000 pounds with sales at 3,083,000 pounds valued at $861,000.

The non-sulfated acyclic esters and ethers in 1956 reached a production figure of 114,200,000 pounds, with sales of 103,487,000 pounds valued at $27,165,000. This group includes glycerol, glycol and polyoxyethylene fatty acid derivatives. Glyceryl monostearate production in 1956 was 12,247,000 pounds with sales of 11,773,000 pounds valued at $3,114,000; glyceryl monooleate production was 7,877,000 pounds in 1956, compared with 3,720,000 in 1955 and 2,070,000 in 1954; polyoxyethyl monostearate production in 1956 was 2,762,000 pounds.

PHARMACEUTICAL FLAVORING

(*Continued from page 751*)

peneless oils or spray dried flavors are preferable in avoiding deterioration, particularly if long storage is contemplated.

The use of terpeneless oils is attended by certain disadvantages. The price is generally high and even though the flavoring agent is quite concentrated and substantially less is required in use, the flavor effect is not always the same as the original. For example, fresh lemon oil has a rich aroma and delicate flavor that are lost in the deterpenation process, the terpeneless oil being harsh and powerful and when diluted lack the finer qualities of the original oil.

Antioxidants have proven valuable adjuncts in the stabilization of essential oils but it is vital to use the antioxidants as early in their history as possible. There is no advantage in adding an antioxidant to an oil in a state of deterioration, as oxidation has already started progressive deterioration usually cannot be halted by this means.

The flavor manufacturer does everything possible to deliver merchandise in top condition but he can hardly be held responsible for the changes that take place as a result of improper handling and storage. Deterioration can practically always be traced to lack of awareness on the part of the user regarding proper handling and storage of sensitive oils and compounds.

Oils, and flavor compounds, should be stored in filled amber-glass bottles at 70° F., and protected from direct light and higher temperatures.

The following essential oils represent those commonly used.

Oil of peppermint—This important oil is more stable than most essential oils since a stable alcohol, menthol, makes up an appreciable portion of the oil. The oil may be stored safely in heavy tin containers but clean amber bottles are preferred.

Oil of clove—Eugenol, the chief constituent of clove oil, will deteriorate slowly under unfavorable storage conditions. Traces of iron may produce undesirable color changes both in the oil and the flavored product. Although safely stored in heavily tin-lined drums, the best container for the oil is glass.

Oil Cassia—Improper storage will convert the aldehydes into the corresponding acids. For lengthy storage the oil should be removed from metal cans and drums and placed in amber glass bottles.

Oil Bitter Almond—Since this oil has a high aldehyde content it should be stored in a similar way to oil of cassia.

Oil of Spearmint—This oil contains a rather high percentage of ketones which will polymerize under improper storage conditions. In order to prevent catalysis as a result of metallic contamination, the oil

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U.S.I. CHEMICAL NEWS

December ★ A Series for Chemists and Executives of the Solvents and Chemical Consuming Industries ★ 1957

U.S.I. Among Winners of Chemical Engineering Achievement Award

The 1957 Award for Chemical Engineering Achievement, presented at *Chemical Engineering's* Annual Award Dinner at the Waldorf-Astoria in New York on Tuesday, December 3, is a group award recognizing the pioneering application of chemical engineering principles and proceses in extractive metallurgy.

U.S.I. is one of 75 organizations in industry and government to share this honor, and is cited for its contribution to zirconium and titanium process technology. The U.S.I. processes for these metals are based on sodium reduction of the metallic tetrachlorides and are believed to be the most economical processes developed to date for the production of metal sponges.

The citations of the Committee of 90 senior educators, under the chairmanship of Dr. Walter Whitman of M.I.T., are limited to the newer metals: uranium, plutonium, zirconium and hafnium, tantalum and niobium, lithium, boron, beryllium, thorium and the rare earth metals. Also included as important to the nuclear industry are aluminum, nickel and titanium.

New Process to Synthesize DL-Piperitone Depends On Sodium Dispersions

DL-Piperitone can now be synthesized from ethyl acetoacetate, a by-product of neoprene manufacture. As against natural piperitone, a synthetic material has the advantage of dependable supply. Consequently an efficient and inexpensive method of commercial production has been sought for some time.

The technique of dispersing metallic sodium in inert hydrocarbon media, developed and perfected over the past several years by U.S.I., is at last providing a practical solution to the problem. A proposed commercial process based on this technique follows:

(1) Sodium and isooctane are agitated together to form a dispersion which is added to ethyl acetate in the mole ratio of 7.3 to 1. The resulting solution is heated.

MORE

Vinyl Heat Stability Improved When ISOSEBACIC® Acid Is Used As Plasticizer Intermediate

New Plant Starting Up To Produce ISOSEBACIC Acid

A newcomer among plasticizer intermediates, ISOSEBACIC acid, is improving the heat stability of polyvinyl chloride films. The table below is based on tests conducted by a formulator of top-grade films for seat-cover use. It gives the comparison between diisooctyl Isosebacate, an ester of ISOSEBACIC acid, and a commonly used plasticizer, diisodecyl adipate.

Comparing columns (1) and (2), it can be seen that heat stability improves 50%, from 30 to 45 minutes, when 15 parts of the Isosebacate replace an equal quantity of adipate. A comparison of columns (3) and (4) reveals that heat stability is improved 100%, from 30 to 60 minutes, when both ester concentrations are raised to 22 parts.

Tests also indicate that ester plasticizers formulated with ISOSEBACIC acid have improved color, odor, and oil and soapy water extraction properties. These properties are important for applications such as auto seat covers, furniture upholstery covers, shower curtains, luggage and handbags.

ISOSEBACIC acid is a mixture of isomers of sebacic acid in about these proportions:

2-ethyl suberic acid 72-80%
2,5-diethyl adipic acid 12-18%
sebacic acid 6-10%

In addition to the vinyl plasticizer application, the material is being evaluated in polyurethane foams, polyamides, polyesters, alkyd resins and jet lubricants.

ISOSEBACIC acid is a product of U.S.I. research. It is derived from butadiene and sodium, both available in unlimited supply. U.S.I. is now in the process of starting up its new ISOSEBACIC plant at Tuscola, Ill.

Diborane Now Produced Commercially; 3 Amine Boranes Being Researched

Diborane, precursor of pentaborane rocket fuel and promising as an intermediate, reducing agent, catalyst and flame speed accelerator, is being marketed in commercial quantities.

According to the manufacturer, physical and chemical properties are now completely determined. Chemical reactions which have been thoroughly investigated include those with ammonia, amines, phosphines, ethers, carbonyl compounds, hydrocarbons, metal alkyds and hydrides, and sodium.

Amine Boranes in Research Quantity

Also available, although in research quantities only, are dimethylamine-borane, trimethylamine-borane and pyridine-borane. Their utilization as selective reducing agents in non-aqueous solvents has been of most interest. They are polymerization catalysts and inhibitors for acrylates and vinyl compounds. In addition, applications as antioxidants and stabilizing agents have been suggested as promising possibilities.

Table of Field Test Data Comparing Diisooctyl Isosebacate Against DIDA as a Vinyl Plasticizer Intermediate

FORMULATION	Parts Per Hundred of Resin			
	1	2	3	4
PVC	100	100	100	100
DIOP (diisooctyl phthalate)	18	18	22	22
DIDA (diisodecyl adipate)	15	—	22	—
Diisooctyl isosebacate	—	15	—	22
Phosphate plasticizer	11	11	—	—
Stabilizer A	2	2	2	2
Stabilizer B	1	1	1	1
Stabilizer C	1	1	1	1
1. Volatility (active carbon method) 24 hrs. at 158 F, % loss	1.38	1.21	0.92	1.07
2. Clash-Berg, Tf, °C	−24.4	−20.0	−23.9	−23.4
3. Heat Stability, minutes stable at 350 F	30	45	30	60
4. S.P.I. Impact Test (Masland) Pass/Fail °F	−20/−25	−20/−25	−20/−30	−25/−30
Gauge	0.019"	0.020"	0.019"	0.021"
5. Germicidal Lamp Test, 16 hrs, tack	slight	slight	slight	slight
6. Blooming, Room Temperature, press polished	O.K.	O.K.	O.K.	O.K.

December ★ **U.S.I. CHEMICAL NEWS** ★ 1957

CONTINUED

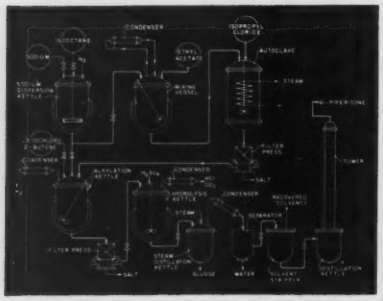
DL-Piperitone

(2) When reaction is complete, isopropyl chloride is added and the mixture is heated.

(3) The resultant slurry is filtered and the filtrate is alkylated with dispersed sodium to form the sodium enolate of ethyl oxisopropyl acetoacetate.

(4) 1,3-dichloro-2-butene in anhydrous benzene is added, and the mixture is refluxed until neutral.

(5) After filtration, the mixture is hydrolyzed with sulfuric acid, distilled and stripped of solvents. A crude, high-boiling dl-piperitone results. Further distillation yields pure dl-piperitone.



With this process, synthesis of DL-piperitone is reported to be commercially feasible.

New Standard Issued on Polyethylene Plastic Pipe

A new Commercial standard for black flexible polyethylene plastic pipe has been established by the Dep't. of Commerce, in cooperation with the Society of the Plastics Industry and the Nat'l. Sanitation Foundation.

The new standard, CS 197-57, specifies that "... the pipe shall be manufactured of virgin polyethylene, that no scrap material has been used, and that it is satisfactory for potable water." It also lists new dimensional tolerances and testing procedures.

Copies are available from Superintendent of Documents, U. S. Government Printing Office, Washington 5, D. C. for 10¢ a copy.

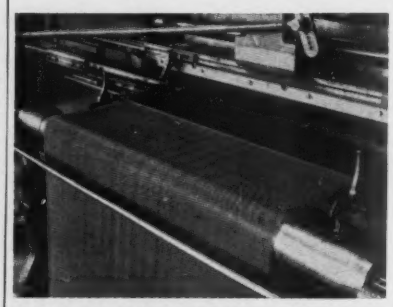
Corrosion-Resistant Mesh Is Now Produced with Improved Titanium Wire

The fabrication of titanium wire cloth now has reached a production basis. This is due primarily to improvements in quality of wire, which until recently lacked the needed uniformity and elongation, and had a tendency to work-harden rapidly and gall on metal-to-metal contact.

With wire-forming problems licked, and cloth being fabricated efficiently with high-purity and ductile grades of mill product, new applications are developing rapidly. Although noted for its high strength-to-weight ratio the biggest advantage of titanium in wire cloth form is its unique corrosion resistance. The metal has a corrosion rate of only .000001 inches per year in sea water, and is not subject to stress corrosion cracking in sea water or sea air.

Titanium wire cloth is being fabricated more and more into filter screens, catalyst screens or similar assemblies, where it handles mineral acid solutions, sodium hypochlorite, chlorides of all kinds, organic acids, alkalies and other reagents, with superior resistance to corrosion.

Several companies also report ability to make woven screen from zirconium wire, for those applications where zirconium corrosion resistance is superior to titanium.



Titanium wire cloth being woven (photo courtesy Cambridge Wire Cloth Company).

TECHNICAL DEVELOPMENTS

Information about manufacturers of these items may be obtained by writing U. S. I.

A silicone rubber which vulcanizes at room temperature has just been introduced for encapsulating, potting, sealing and caulking. Retention of rubber-like properties from —70 to 500°F is claimed. **No. 1301**

"The Rudiments of Feed Formulation", a 6 page reprint reviewing the industrial sources of animal feed constituents, the formulation of mixed feeds and the energy and nutrient values found therein, is now obtainable on request **No. 1302**

A new monomeric ester-type plasticizer for vinyls and cellulosics is described in a 4-page data sheet now available. Chemically it is di-2-ethylhexyl Isosebacate, reported about ⅓ lower in cost than the corresponding sebacate. **No. 1303**

Entirely new series of high molecular weight disazo red pigments for PVC and latex paints is said to combine the strength and brightness of organic pigments with the stability normally associated with inorganic pigments. **No. 1304**

Thioglycolic acid — its properties, reactions and uses — is described in a new 20-page catalog now available free of charge. An extensive bibliography of relevant patents and trade paper articles is included. **No. 1305**

Ethyleneurea (2-imidazolidinone), a new chemical, is now on the market. Used to make lacquers, varnishes, finishing agents, adhesives, plasticizers. Forms highly polymerizable vinyl and other derivatives. **No. 1306**

New series of zinc rich coatings to protect steel from the atmosphere and in marine and chemical use has been developed. Applied by brush or spray. Are said to be tougher, tighter, better bonded than old-type zinc coats. **No. 1307**

New adhesive for polyurethane foams is made with new, extremely fast-drying polymer, is said to lose its depression tack faster than any other material on market. Permits bonding with an adhesive as soft as the foam itself. **No. 1308**

A gas analyzer for measuring trace hydrogen, oxygen and nitrogen in metals has just been introduced for use right in the mill. Claimed to be only apparatus on market for both vacuum fusion and extraction. **No. 1309**

Pyridine N-oxide can now be obtained in commercial quantities. This exceptionally reactive derivative can be used to prepare many other pyridine chemicals valuable to the drug, dyestuff and allied industries. **No. 1310**

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Animal Feed Products: Calcium Pantothenate, Choline Chloride Products, MOREA® Premix, Special Liquid Curbay®, DL-Methionine, Niacin USP, Riboflavin Concentrates, Vitamin B_{12} and Antibiotic Feed Supplements, Vacatone® 40, Vitamin D_3 and K_3 Products, Antioxidant (BHT) Products, Special Mixes, U.S.I. Permadry Products (Sealed-In Vitamin A).

Inorganic Chemicals: Ammonia, Caustic Soda, Chlorine, Metallic Sodium, Sodium Peroxide, Sulfuric Acid.

Metals: Titanium Sponge, Zirconium Sponge, Zirconium Platelets, Hafnium Oxide, Hafnium Sponge.

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should be stored in amber glass containers.

Oil Sweet Birch and Oil of Wintergreen—These oils possess a high ester content and the esters hydrolyze in time to the corresponding alcohols and acids. In order to retard deterioration, proper storage in heavily tinned metal or glass containers is essential.

Oil of Anise—This oil comprises in large part the phenol ether, anethol, which is relatively stable. The oil may be kept safely in heavily tinned containers.

Citrus Oils—This group embraces very important flavoring agents among which are lemon, orange, lime and grapefruit. All these oils contain appreciable amounts of terpenes which, as unsaturated hydrocarbons, have a high affinity for oxygen of the air. They are for that reason extremely perishable and must be kept in well-filled, tightly-stoppered containers.

The turpentine-like odor and flavor which develops after citrus oil oxidation is readily detectable in the finished product. All citrus oils deteriorate in time and it is difficult to correlate oil quality with keeping quality, but there is a tendency for the better grade of oil to resist deterioration longer than the cheaper grades. In general, the fresher the oil, the fresher the terpenes and the better the keeping quality.

A simple means for the evaluation of the relative keeping quality of citrus oils has been utilized for screening a considerable number of samples from various suppliers. The test comprises the addition of 1 ml. of oil to 20 grams of anhydrous dextrose. The oil is uniformly distributed throughout the powder, placed in 2 oz. wide mouth clear glass bottles and capped. The test bottles are stored in an illuminated (100 watt clear glass bulb) incubator at a constant temperature of 20° C. The contents are examined organoleptically each week until deterioration is noted.

This simple test provides a yardstick by which relative keeping quality may be observed under controlled conditions. The behavior of a large group of flavors under these conditions will supply valuable information which can be utilized as a basis for predicting storage behavior. By accelerating deterioration, it can be learned which oils stand up best under the conditions imposed. Fresh, top quality oils generally stand up best. Partly deteriorated oils autocatalyze rapidly regardless of initial quality and the flavor defect can be detected readily by this test.

As a general rule, all perishable oils should be stored in well-filled clean, dark amber, tightly stoppered bottles. After use, the bottle should be scrubbed clean with a good detergent and then rinsed and dried thoroughly. Bottles with plastic screwcaps containing aluminum liners are recommended. Cap liners must be replaced with fresh aluminum inserts after use. It is advisable to employ the same bottles for the same flavor type.

Subdivide bulk oil shipments as soon as possible into smaller containers, the latter approximating vat size quantities. Heavy galvanized or stainless steel drums may be utilized for prolonged bulk storage so long as

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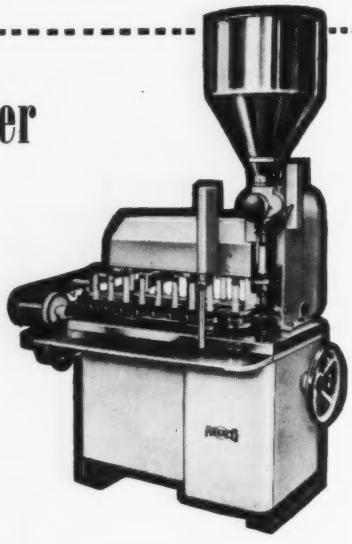

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no appreciable withdrawal is made (resulting in increased head space). Once a withdrawal is made, the drum should be emptied into dark amber bottles as soon as possible. A systematic procedure for rack storage of all bottles will prove convenient.

All utensils in contact with essential oils at any time during handling should be carefully examined as possible sources of metallic contamination, particularly copper and iron. Glass, heavily tinned, or stainless steel utensils are recommended for this purpose.

Careful supervision of the flavor room is essential to assure proper filling, storage, weighing, dispensing and batch mixing. Cleanliness and neatness are essential to flavor handling and should be applied to every phase of the operation.

The simplest approach to the formidable problem of flavoring extremely unpleasant oral medicaments is to capsule or tablet the product. Apart from the difficulty often experienced by children and the aged in swallowing tablets and capsules, there are therapeutic considerations which may preclude this form of administration.

Taking advantage of the fact that lowering the solubility of a bad-tasting drug usually results in a reduction in unpalatability, finely divided drug suspensions or emulsions have been prepared in media with poor solvent action. Preparation of the drug itself in specific physical form such as fine crystals instead of powder in some instances aids in reducing solubility. The suspending medium itself must be free from taste, as this may present an additional flavoring problem. A multi-sulfa oil emulsion defied all previous efforts to mask the pronounced unpleasant taste, even though the multi-sulfa mixture consisted of compounds manufactured with reduced solubility in mind. The unpleasant taste was traced to the oil base which, because of its unsaturated nature, deteriorated rapidly. When this took place, the solubility of the multi-sulfas apparently increased, which contributed further to the bad taste. Simply by replacing the rancid oil with a stable type, the flavoring of the product became a relatively simple task.

A further step in reducing unpleasant tastes in medicinals is to prepare derivatives of a drug without altering the basic pharmacologic action. Aspirin is bitter to most people; its counterpart salicylamide, because of its lowered water solubility, is relatively tasteless.

The most common method for modifying objectionable tastes in orally administered drugs is perhaps the oldest and that is the use of flavors. Flavors are supplied in a number of forms, the most concentrated being the flavor oil consisting of synthetic aromatics, essential oils and isolates, without prior dilution. Invariably, these are intensely powerful mixtures and further dilution is required in order that they may be easily measured and distributed thoroughly in preparing a flavored pharmaceutical. Dilution may be achieved by the use of ethyl alcohol, propylene glycol

or water in conjunction with a suitable emulsifier which may be either a surfactant or a gum or a mixture of both. The dispersing medium for the medicinal is a factor in the selection of a proper diluent for the flavor.

Each pharmaceutical product must be flavored individually and experience plays an important role in achieving the most desirable effect. While there are no hard and fast rules to cover every type of perparation, some consultants and flavor manufacturers have acquired considerable experience in working with numerous products and the pharmaceutical manufacturer will do well to seek their assistance in this connection.

Pharmaceutical products fall into a number of general groups and for the sake of simplifying flavor selection, those flavors which have enjoyed good success in each group can also be classified. This is by no means an exhaustive list and it is intended only to give sufficient background for experiment.

Geriatrics—Geriatrics usually comprise alcohol mixtures of vitamins, minerals, iron, protein hydrolysates, vegetable tonics and mineral tonics. Low proof alcohol-sugar mixtures provide the basis for universally popular cordials and liqueurs. Flavors of this type are ideally suited for geriatric preparations.

Geriatric Flavor Types:

a. Cordials and liqueurs:
   - Anisette
   - Apricot
   - Orange bitters
   - Blackberry
   - Cherry
   - Cocoa
   - Curacao
   - Grape
   - Grenadine
   - Marascino
   - Peach
   - Raspberry
   - Strawberry
   - Violet flowers

b. Geriatric flavors for general use:
   - Anise
   - Chocolate mint
   - Orange
   - Rootbeer
   - Sweet Cherry
   - Wild cherry
   - Peppermint

Vitamin Preparations—These comprise by far the largest single group of pharmaceutical products, and may be either straight vitamin mixtures or combinations with supplements such as liver, yeast extracts and protein hydrolysates.

Particular attention must be given to the selection of aldehyde-free flavors for use in preparations containing Vitamin B_{12}.

Flavors useful in vitamin elixir preparation are:
- Anisette
- Raspberry

(Continued on next page)

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Rootbeer
Sherry
Strawberry
Vanilla

Antacid Preparations—Included in this group are products based upon calcium carbonate, sodium bicarbonate, aluminum hydroxide, and magnesium carbonate, usually in tablet form. Sweetness level, texture and ease of dissolution in the mouth are important considerations.

Suggested Flavors for Antacids:

Peppermint
Spearmint
Wintergreen
Cherry
Vanilla
Licorice
Cinnamon
Coconut

Antibiotics—This highly important group covers a large selection of products with extremely bitter tastes, dispensed as tablets, troches, suspensions and solutions.

Suggested Flavors for Antibiotics:

Cherry
Orange
Banana
Pineapple
Chocolate-Vanilla
Lemon
Rootbeer
Licorice
Raspberry
Strawberry
Lime

Oral Fat Emulsions and Fatty Oils—This group includes straight oils, dietary supplements for large caloric intake and the newer essential fatty acids. The characteristic oily note sometimes lends itself to novel and interesting flavored effects. The use of vanilla and ice cream flavors offers unusual possibilities in conjunction with gum stabilizers to provide a pleasant flavor effect.

Flavors suggested for Oils and Fat Emulsions:

Cocoa-fudge
Chocolate-vanilla
Cherry
Root beer
Vanilla
Black walnut
Coconut
Cherry-vanilla
Chocolate-malt
Toasted coconut
Strawberry
Raspberry
Peach
Pistachio
Maple-vanilla
Butter

Barbiturates—Usually in elixir form, these medicinals tend toward bitterness. Sweetening agents are almost always required in conjunction with flavoring compounds. Fruit flavors, particularly citrus types, work rather well with this group. Sweetening agents may be cane sugar, sodium cyclamate, calcium cyclamate and saccharin.

Suggested Flavors for Barbiturates:

Lime
Lemon
Orange
Mint
Strawberry
Raspberry
Anise
Fruit compote
Tangerine

Sulfa Preparations—These medicaments may contain sulfadiazine, sulfamerazine, sulfanilimide and sulfaguanidine, most commonly in aqueous suspensions.

Suggested Flavors for Suspensions and Tablets:

Malt
Root beer
Vanilla
Orange
Lemon
Lime
Raspberry
Anise
Fruit Compote
Coconut

NOTE: Lemon flavors work well in conjunction with traces of citric acid.

Analgesics—This group embraces aspirin, salicylamide, acetanilid, cinchopen and acetophenetidin.

Suggested Analgesic Flavors:

Orange
Lemon
Anise
Root beer
Banana
Wintergreen
Cachou

Distasteful Drugs—In this group fall protein hydrolysates, vasodilators, hypotensive agents, and certain alkaloids (homatropine methyl bromide). Sweetening agents are vital to success.

For making bitter and other unpleasant tastes the following flavors are suggested:

Spearmint
Peppermint

Mint Anise
Lemon
Licorice
Raspberry
Fruit compote
Cherry
Chocolate
Cachou
Cinnamon
Peach-Orange

In conclusion, the flavoring of an unpleasant tasting pharmaceutical preparation requires skill, a large battery of samples, and much patience. As a final word of caution, the interaction of flavor and active ingredient cannot be predicted; stability tests should always be done on the completed product with the flavor added. Analytical and subjective tests should then be run to determine that neither the medicinal nor the flavor has been adversely affected.

MEDICAL RESEARCH FOR PROMOTIONAL PURPOSES

(Continued from page 753)

The use of a "personal communication" of this nature is certainly not a sales asset. It belongs in the classification of "testimonials" upon which the industry has looked with disfavor in the past. You cannot expect the medical profession to respect it.

d) **Control of Experiments.** Has the investigation been carried out under controlled conditions; that is, have the results been compared with known standards?

Have objective criteria been used?
Have appropriate laboratory tests been made?
Has the action been compared with that of other drugs?
(Not every firm has the courage to do this).
Has the drug been used as the sole therapeutic agent or is it one of many employed?
When applicable, has a double-blind study been made or do the data merely represent the "impression" of the investigators? It is now generally agreed that double-blind studies are needed for the evaluation of many drugs, especially such as the tranquilizers, analgesics and others.

If the clinical investigations indicate your drug to be superior to others, you have a real story to tell; if your compound is equal in effectiveness you can still be optimistic, depending upon the ability of your sales force; if your drug is only slightly inferior in effectiveness not all may be lost, but you have to review your sales assets more thoroughly. Maybe you have special dosage advantages to offer, or less side-effects, or a lower price; or maybe your market studies indicate that the competing drug is not sold to a large extent in areas where your firm is well established: the South, or the Middlewest.

e) **Scope of Clinical Studies.** In how many

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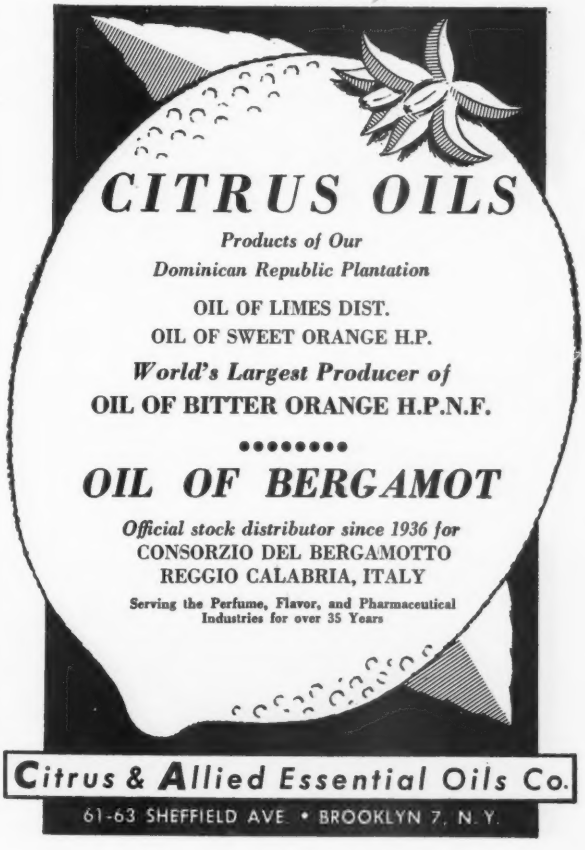
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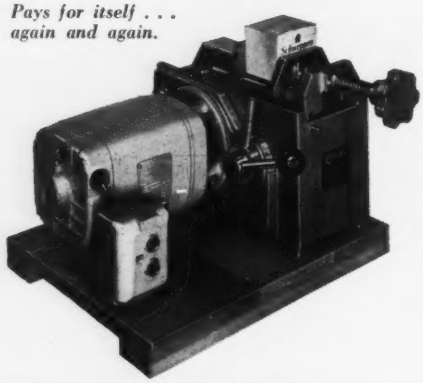

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patients has the drug been used? About five years ago everybody was crying for investigations in a large group of patients: impress the physician with mass investigations; large series are imperative. Today the pendulum is swinging back. Responsible investigators place more reliance on the thoroughness of an investigation in small series of patients, as for instance, 25 or 50, each carried out by a few independent research workers. Mass use is considered of little interest as far as effectiveness of a product is concerned. For instance, it is regarded as highly suspicious if a physician claims that he has used a new vasodilator in 100 patients suffering from angina. It is asked where he got that many patients, becasue true angina is difficult to diagnose, and requires long-time and careful observation to determine the effectiveness of a drug.

Mass studies in large clinics are of primary value to determine safety and the occurrence of allergic reactions. Because patients vary in their susceptibility to a drug, reactions will only show up in a large series. So, by all means, ask the question: in how many patients has the drug been used? but know why you ask it, because only then can you appraise the sales value of the answer. If you review the recent investigations of Orinase, you will find both the painstaking study carried out in small series of carefully controlled patients and the mass investigation to establish general safety of the drug.

f) **Dosage Schedules.** Does the paper submitted include complete dosage schedule covering both adults and children under all conditions of treatmet? I have occasion to review many hundreds of clinical reports yearly and I find frequently that dosage instructions are very scanty. Dosage instructions are one of the most important components of a clinical report on a new drug. The more specific they are the easier it will be for the practicing physician to use the product successfully. Completeness in this respect is a great sales asset. There is no reason why you should not ask your medical department to insist upon this, and in your evaluation of the product you should stress the availability of such information.

g) **Side Effects.** Does the drug produce any secondary effects, i.e. skin rashes, dizziness, etc.? In what percentage of patients receiving the drug has this been observed? It is best to call these to the attention of the physician, so that he is forewarned, and not surprised or disturbed, when they do occur.

h) **Contraindications.** What are the contraindications to the drug? Not only the FDA and official medical organizations, but also the directors of clinical research of pharmaceutical manufacturers are insistant upon the enumeration of contraindications of a drug. The mentioning of these is not a handicap but in my opinion a sales asset, because in this way you teach the physician how to use your drug correctly.

I shall now discuss a few concrete examples by way of illustration. The first example represents a clinical report on a new drug that has not yet been marketed.

Investigators. The study was carried out at a hos-

pital associated with one of the universities. One investigator is a professor of clinical medicine and the other is a resident of this particular division of the hospital.

Products Used. Five different preparations were employed since 1943 and comparisons with the new product are presented.

Comparison with three *rapid and short-acting drugs.* Their use is discussed but no actual data are presented. It is stated, however, that the previously used compounds produce a peak and valley type of curve which is not desirable.

Clinical Evaluation in about 1500 Hospital Patients. This includes both in- and outpatients. The new drug was used in five different disease conditions. Its effect was observed during a nine months' period, and measured according to five clearly defined objective criteria.

There is a detailed discussion of the results obtained, and charts are presented for each of the five different conditions in which the drug has been used as the sole therapeutic or prophylactic agent. These charts should prove very useful for promotional purposes. It might have been advantageous, however, if the percentage of successes and failures had been added. It would also have proved of value for promotional purposes if similar charts of the previously used short-acting drugs had also been presented, because that would have given a better comparison of the value of the new drug with older forms of therapy and the whole presentation would have been more rounded-out and impressive. The data for such charts of previously used drugs could possibly have been extracted from the hospital records. As I previously indicated, the authors only make a general comment on the undesirable peak and valley effect of the shorter-acting drugs which had previously been employed, but do not present actual data, assuming that these are widely known.

Comparison in 290 outpatients with two other long-acting drugs. All three products are chemically related. The use of the previously employed drugs covers a period of one to ten years. In this instance exact data on previously used drugs are given, and the tables represent percentage figures as follows:

	#1	#2	*New Drug*
Excellent and Adequate	47.6	18.9	72.2
Fluctuating	40.0	68.5	25.0
Resistant	12.4	12.6	2.8

This comparison definitely suggests superiority of the new drug and will impress the practicing physician. The authors conclude that the new product is a drug of choice for long-term therapy.

Dosage Description. The authors emphasize that each type of patient represents its own therapeutic problems. They have therefore cited actual dosage schedules which can be used as a guide for the treatment of each type of condition. This is most valuable information because it teaches the physician how to use the drug effectively under a variety of conditions.

In conclusion we might therefore say that although

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this report is not ideal in every respect, it presents very worthwhile features of a new drug which can be used effectively for sales promotion, provided the results obtained can be confirmed by other investigators, and provided no new and more effective drug is made available for therapy prior to the marketing of this new compound.

The next example presents an entirely different situation. It is a review of pharmacologic and clinical data that were made available some time ago by a manufacturer in his first announcement of a new drug to the physician.

The *bibliography* of the presentation referred only to "personal communications" from individual physicians. No reference is made to any data published in the medical literature.

Pharmacologic and Toxicologic Studies. These had been made in the firm's laboratory. There are no data from which the reader can draw his own conclusions, but only several categorical statements describing the pharmacologic results obtained are given. There is also a theoretical discussion of the site of the action of the drug. On the toxicity studies made with the compound somewhat more detailed data are presented. This entire presentation is similar in style to those we used to see in announcements of new drugs by European pharmaceutical manufacturers in the 30's and 40's. But these firms too have learned, and now are publishing data in detail in appropriate journals for critical analysis by other independent research workers.

Clinical Evaluation. This was carried out by five investigators who are all specialists in their particular fields and who all reside in the same area of the country. The manufacturer's announcement describes the use of the product in some 70 patients, which suggests an average of 14 patients per physician. But when we analyze the data still further we find that the product was used in 5 distinctly different conditions. This still further reduces the number of patients in whom the drug was used for a specific disorder. In one disease condition the drug was used by 4 investigators in 5 patients, or 1¼ patient per physician!

The responses ascribed to the drug are entirely subjective, and no attempt has been made to use a blind study or objective criteria. The patient felt better or he did not. That was it.

I have used this as an illustration primarily to show that it had evidently been decided to market the drug at a time when no more data were available than those given in the manufacturer's first announcement to the physician. You would, therefore, have been called upon to review this material prior to marketing. If you had used the criteria I enumerated earlier, and if you had also weighed the competitive situation, which is quite keen in this field, I doubt that you would have recommended marketing of the drug at that moment. The supporting evidence is just not strong enough, and your function would be to ask for an extension of the clinical evaluation to strengthen the competitive situation of the product, and to learn more as to how its action compares with that of similar drugs already available.

Personally, it does not seem fair to the manufacturer, to the physician, or the patient, to market a new product on the basis of such relatively scanty clinical evidence of its usefulness as a therapeutic agent.

It is not fair to the manufacturer, because—

1) Whatever he thinks of the capability of his research staff, it is an old axiom in scientific work, that original studies of one group become valid only if they have been confirmed by others. Too many things can go wrong in experimental work.

2) In this case clinical evaluation has not been carried out under controlled conditions. Use in larger series of patients may reveal inadequacies previously not noticed, and there are no comparative data with other products.

3) The occurrence of side effects, of which some have been observed even in this small series, may increase appreciably during more extensive use.

4) An initial sales success based upon extensive promotion may turn into an expensive failure at a later time.

It is not fair to the physician, because—

He is being asked to prescribe to his patients a new drug whose efficacy requires confirmation. Therefore he does not know whether he is prescribing the most suitable and active product for his patient. The individual physician is actually being asked to carry out experimental work with a new drug, for which he has no facilities.

It is not fair to the patient, because—

While new drugs have to be tried without exact knowledge of their effectiveness during a clinical trial period, the patient should be able to expect that his practicing physician will use a new drug on him only if it has undergone adequate clinical trial, and appears to be equal or superior to others.

Compounded Products. I have discussed with you two examples of two new drugs which are single chemical entities; but the majority of new drugs, about 70 per cent, put on the market yearly by the industry is represented by so-called compounded products. It is my observation, based on a rather extensive and continuing review of the literature, that very few combination products are subjected to clinical evaluation. The promotion expense for such drugs is usually not lower than that for a really new drug, and therefore the cost of failure is just as substantial. We all know that the cost of product failure is very high, and, without citing any exact figures, it has been my observation that an appreciably higher percentage of compounded products fail than of new single drugs.

It is in the field of marketing compounded products that market research can perform a real service, that is, by insisting that such combination products, if they are in any way new and not mere duplications, be

subjected to the same clinical evaluation as a new single drug. It is you who are asked to make sales forecasts, and it is you who are assuming the responsibility for predicting success or failure. Your voice will be respected by management, if you can back it up by case histories of other products, whether of your own or those of other firms. If you are told that it is too expensive and time-consuming to carry out a clinical evaluation with these preparations, you can always state that such expenditure is only a small part of the funds that have to be provided for a national promotion of the product. Some firms are using test marketing for this type of product evaluation, but in this highly competitive and fast-moving market there are only a few manufacturers that carry out a test campaign in a limited area. These will help in cutting down disappointments, but adequate clinical data are a much greater sales asset for national promotion.

Communication with Medical Research. I said at the beginning of this paper that your department is frequently the first contact a new product has with the harsh commercial world, so give it a chance to become acquainted with all aspects of it. Let the people who handle sales and advertising departments take a look at it too. I feel that medical research is also promotion, because it provides the data which will enable the physician to use the product effectively. That is where science and commerce meet in the pharmaceutical industry, and you can be the go-between between the two.

One of my prime interests in the industry is to prepare products for marketing, and I have always felt that a close liaison between the professional man and the salesman is of great importance in the early stages of product development. As market research people, you know the competitive situation, because you follow it closely, and your sales division knows what will aid it to put a product across. For all these reasons it is of first importance that you should have good and constant communication with your medical research division.

Some of you may think that it is not up to you to ask your research departments questions as to evidence of the efficacy of your product; that such matters are obvious to them, and that your query might be considered unwanted interference. I do not think that you will encounter this problem if you limit yourselves to those few basic questions of evaluation we have reviewed today, and if you use the necessary diplomacy in asking them. Life is made up of checks and balances, and while the sales division of which you are the advance guard expects adequate data from research, research will see to it that the information they supply is used correctly and effectively for the guidance of the physician and the benefit of the patient. New drug development and selling is a cooperative effort, and our industry is fortunate to be able to combine for this purpose professional and commercial talents.

Summary. To recapitulate, then, these are the

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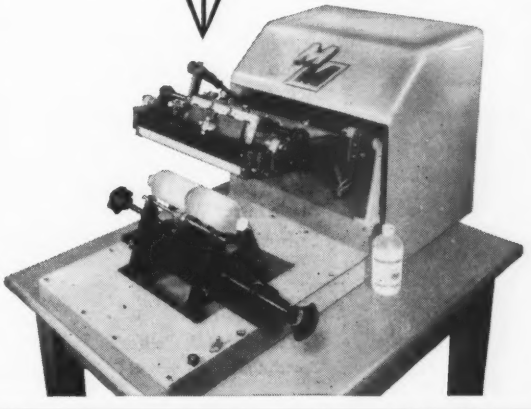

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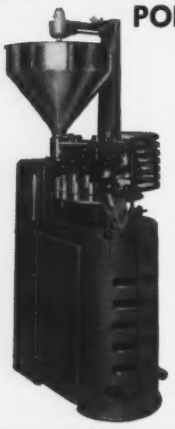

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major sales assets one should look for when evaluating research reports for promotional purposes:

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2) Reputation of clinical investigator.
3) Location of investigators.
4) Suitability of reports for publication in a medical journal.
5) Thoroughness of investigation; is it carried out under controlled conditions with adequate objective criteria, and are the limitations of the drug clearly stated?
6) Effectiveness in comparison with other drugs.
7) Complete dosage instructions for all conditions and for various age groups.
8) Safety of drug, with listing of side effects.
9) Listing of contraindications.

Outlook. I offer a few general recommendations for the overall activities of market research:

If market research aspires to be a profession, and I believe it is a profession, it must be prepared to carry out creative research in the development and marketing of new products. By creative research I mean the constant study of changes in medication and product trends; the observation of the type of promotion and expenditure used by the industry; the review of new product development by other firms; a study of which products have succeeded and which have failed, and for what reasons.

There are fashions in medicine as in anything else in this world, and market research studies can determine their beginning and predict their end. To present useful and valid data such investigations must, however, be carried out over a period of years. A few months' or a year's data are much too incomplete. These studies will enable market research to come forward to management with constructive recommendations for the development and marketing of new products which will be accorded the respect of the medical and sales departments.

As John Ray the great naturalist said in 1691, in The Wisdom of God Manifested in the Works of the Creation: "True it is, many of the greatest inventions have been accidentally stumbled upon, but not by men supine and careless, but busy and inquisitive." So let us be busy and inquisitive about everything that has been and is going on in medicine and in the industry serving it, let us determine the reasons why, and we shall come up with unexpected answers that will guide us in the future to success and rewarding accomplishments.

MERCHANDISE INCENTIVES

(Continued from page 763)

this is an effective way to stimulate competition among our sales force.

As a final incentive, the three leaders in each district earned bonus points at the end of the campaign: top man received an additional 5000 points, second highest man an additional 2500 points and the third highest, an additional 1500 points.

Of the 95 per cent of the men who won prizes, more than 50 per cent won what would be considered superior prizes. Forty of the top point-earners in the Antivy campaign earned between 40,000 and 60,000 points.

The success of the Antivy campaign can be measured in terms other than increased sales and achieving our three goals. We at Ciba believe that the "Over-The-Counter" merchandise incentive campaign also gave us better morale and a better selling team.

TESTING THE EFFECT OF SOAPS AND DETERGENTS ON LIVE HUMAN SKIN

(Continued from page 756)

generated by the skin by measuring the wettability of the skin before and immediately after, as well as many hours after the removal or extraction of these compounds from the skin.[28] A. Szakall[35] came to the same result by repeated water extractions of one and the same skin area and the quantitative determination of the extractables in each extraction. The water-soluble compounds in the hornified epithelium can be looked upon as physiological substances of the skin.

Detergents and, specifically, alkaline detergents can cause an increase in water content. This is represented by a swelling of the skin. Since the swelling is the first step to chemical hydrolysis of proteins, the swelling of skin protein has been studied widely.

Determinations of swelling have been performed on isolated skin materials and keratin materials with the well known methods of colloid, textile and leather chemistry. On the living human skin, however, swelling tests are very difficult to perform. As far as we know the only method described so far is one of Peukert and Greuer.[36] This method uses the principle of the quantitative determination of the inner reflection of a light beam radiated on the skin surface. The inner reflection is measured by fixing a light source at the skin surface and light tight separated from it is a built in circular photo cell. The experimental set-up is similar to the above-mentioned instrument of Hertzman for the measurement of erythema. The authors state that their instrument is based on the erythrometer of Buttner. According to the paper, the swelling of the skin is directly related to the photocurrent in the photo cell. Differently expressed, the higher the photo current the more swollen the skin.

Sebum Levels

Another bad effect on the skin surface can be caused by detergents. This is related to changes of the normal sebum level of the skin. It is generally known that one of the biggest disadvantages of the modern detergents is their strong defatting property. The determination of the intensity of the defatting as well as the time the skin needs to recover to its normal sebum level after the de-fatting is therefore of greatest interest. Besides the total of "solvent solubles" on the skin surface, the acid number, iodine number and ester number as well as the cholesterol content of the solubles have been

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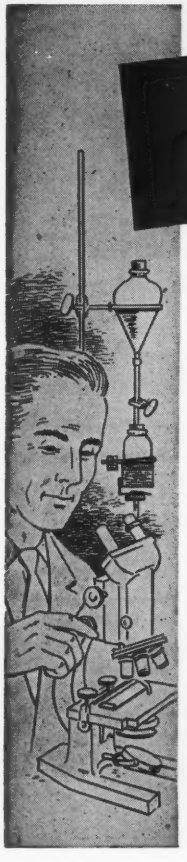

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determined. Carrie[37] uses a funnel which he fixes on the skin with its wider opening to collect sebum from the skin surface. He uses a funnel with the widest opening of 2.9 cm. to cover the total of 26.4 sq. cm. of skin. He places petroleum ether in this funnel and defats the skin for ten minutes. An aliquot part of the petroleum ether-sebum solution is pipetted out of the funnel and titrated with 0.1 N chromic acid. This titration is based on the fact that fats reduce chromic acid. For the cholesterol content a different sample is taken. After the evaporation of the solvent, the fat is saponified with alkali and the cholesterol is then extracted with chloroform. In the chloroform solution the cholesterol is determined by the Liebermann-Burchard color reaction. (Acetic-acid-anhydride plus concentrated sulfuric acid equals green color.) The iodine-, acid, and saponification numbers are checked according to methods of normal fat analysis but adapted to the small quantities resulting from skin surface extractions.

Hermann and Prose[38] use a glass vessel similar in shape to an eye cup, open on both sides, for the collection of the ether solubles of "the skin surface." They evaporate the ether in aluminum foil dishes and weigh the residue. They distinguish between three skin fat levels.

"Casual Level" is the amount of skin fat extracted from untreated areas.

"Total Level" is the amount of skin fat extracted from skin areas which had been protected from contact with the environment for 24 hours previous to the extraction.

"Retained Level" is the amount of skin fat extracted from a skin area which had been wiped in a certain manner previous to the extraction.

These authors confirmed the results of earlier work, namely, that the fat secretion on the skin surface reaches a saturation point and then stops.

Kirk and Effersoe,[39] by using a similar method, have found there is no difference in the influence on the fat level of the skin between soap and detergents.

A fast method of orientation about the sebum level of the skin surface is described by Brun, Enderlein and Krull.[40] These authors press pieces of filter paper on the skin and expose them to osmic acid vapors. The osmic acid stains the paper more or less black depending on the sebum content of the paper. If standard papers are prepared and the test papers compared with those, this simple and fast test becomes semi-quantitative.

Most scientists find that one to one and one half hours after the extraction the normal sebum level of the skin surface is restored.

Changes which the sebum undergoes on the skin by the absorption of soap can be analyzed according to Ramsey and Jones.[41] They measure the spreading area which a monomolecular film of the ether extract of the skin surface occupies on a water surface. Normal sebum always occupies, according to these authors,

the same spreading area. Every deviation from this normal spreading factor shows changes of the skin fat.

The influence of detergents and soaps on the skin has also been studied by investigating the chemical changes the skin substance or, precisely expressed, the horny layer's proteins undergo.

Scott and Lyon,[42] as well as Scott and Flesch,[43] determine the increase in free, bound and water soluble sulfhydryl groups of the stratum corneum before and after the treatment with detergents and soaps. They find that there is an increase in sulfhydryl groups after the treatment with soaps and detergents compared to the treatment with plain water. They believe that these chemical changes of the skin protein are probably partially responsible for the occurrence of housewife eczemas.

Patch Tests

Generally, however, the eczematogenous properties of the detergents are tested with the well known patch test. Technique and value of this method as prophetic patch tests have very often created scientific discussions. This resulted in several recommendations for better techniques. For example, Fernstroem[44] recommends a so-called "pressure patch" which gives a better contact and fixation of the patch on the test area. This pressure patch consists of an 8 x 8 sq. mm. absorption paper covered by 21 x 21 sq. mm. of rubber, foil or cellophane, which is then covered by a little cube of foam rubber 19 x 19 x 4 mm. The whole patch is sewed to a unit with a few stitches and then fixed with adhesive on the skin. The author states that with this type of patch he got positive results with concentrations of test material where a common patch was always negative.

To adopt patch tests to practical use conditions, Shelansky and Shelansky[45] describe the so-called "repeated insult test." In this test the patch is applied for 24 hours. After the removal of the patch the skin area stays uncovered for 24 hours and is again patched for 24 hours etc. for a total of 30 days. After the 30 days a recovery time of two weeks is given and then a patch is again applied for 48 hours. This is done to be able to find sensitization. After each test is removed the skin condition is observed and notes are made. In this way the fatiguing of the defense mechanism and at the same time sensitization of the skin can be detected.

There are many warnings in regard to mistakes which can be made in the performance and the evaluation of patch tests. Some of the possible sources of mistakes are, for example: The choice of the right concentration of test material, the number of testers, the adaptation of the technique and the material in question and the biggest source of mistakes is misinterpretation of the reaction. In this connection, Pleuss'[46] remark that neutral detergents give much less positive reactions in a patch test than soaps is very interesting. Since neutral detergents, however, very often cause eczemas, he believes that their well known de-fatting action is the source of toxic damage which secondarily

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results in the eczema. This example proves the importance of an intelligent interpretation of the test results.

Burckhardt's alkali resistant test also belongs in this group of methods. Eight drops, one after the other, of 0.5 N sodium hydroxide solution are brought into contact with the same skin area. The number of drops which cause a skin reaction is taken as the measure of the alkali resistance of the skin.

For irritation testing as well as sensitization testing, animal tests are used very often. It should, however, be kept in mind that animal experiments for skin tests have only a limited value. For the testing of detergents and soaps, specifically in shampoos, the rabbit eye test has been widely used. In this test a drop of the pure or diluted detergent solution is instilled in the conjunctival sac of one of the two eyes of a rabbit. This drop of detergent solution is either left in the eye or, to approach more normal use conditions, it is rinsed out of the eye with a given amount of water. The changes the eye undergoes are compared with the untreated eye and observed after 1, 24 and 48 hours and then daily up to 7 days. Draize and co-workers[47] have published a paper and point system for the evaluation of the eye reactions. The same group has also recommended skin tests on animals. In this test 10-20 per cent of depilated skin surface of the animals is brought into contact with the test material in geometric dose levels. Some of the animals are treated on intact skin and some are treated on skin which was abraided previous to the test. The test materials are placed in rubber sleeves which cover the body and then stay in contact with the skin for 24 hours. The evaluation is done on a point score too. After the test the animals are kept in single cages for at least two weeks for further observation. Body weight, food consumption and general symptoms are noted daily. The urine is tested for protein reducing substances, blood pigments, etc. Also, changes in the blood composition are checked. Finally, the skin of animals which died during the observation period or directly after the skin test are checked histopathologically.

A test called "acute toxicity" is one in which about 10 per cent of the depilated body surface is brought into daily contact with relatively large doses of the test material for 20 days. Another "90 day experiment" requires the same treatment, but for a period of 90 days. In all these tests the mortality in addition to all the other observations mentioned above are recorded.

Also, patch tests on depilated rabbits as well as on guinea pigs are recommended.

For the testing of sensitivity, the injection test described by Landsteiner and Jacobs[48] on guinea pigs is recommended. In this test 0.05 c.c. of a 0.1 per cent test solution is injected intracutaneously in a skin area of 3 to 5 sq. cm. Every second day 0.1 c.c. of the same solution is injected in the same skin region. This is continued until a total of 0.9 c.c. of the solution has been injected. Two weeks after the last injection a new injection of 0.05 c.c. of a freshly prepared solution is made. Twenty four hours after this injection the diameter, height and color of the reaction is noted and compared with the reaction of the first injection. The degree of sensitivity is the difference between the first and last observations.

O. Kuhn[49] has published an entirely new method for the testing of detergents. He implants little pieces of agar which contain the detergent, under the skin on the back of mice. The reaction is judged by clinical observation as well as by histological observation.

To clarify the question of the influence of washing agents and detergents on the skin, the time of contact as well as the number of repeated contacts is of extreme importance. The question of whether the detergents are substantively absorbed on the skin and remain there longer than desired could, however, first be cleared up by the use of radioactive masked detergents. With radioactive sodium and bromine, masked soaps and detergents, Hopf and Brumeister[50] find that in spite of rinsing the skin, relatively large amounts of detergents remain absorbed on the skin. The most surprising result is, however, that the presence of detergents on the skin can still be demonstrated five days after the test even if normal washing and rinsing is used. After five days quantities of one hundredth of the used test quantity of 0.1 mg. per 1 sq. cm. are still present.

I have mentioned and briefly described a number of test methods which are used for the investigation of the influence of soaps and detergents on the skin. I would like to emphasize that one single method used to study the influence of detergents on the skin can only give a very limited answer. Only the combination of as many suitable methods as possible can, to a certain extent, throw light on what takes place on the skin surface.

However, to give us a total true picture about what happens on the skin surface in contact with detergents and soaps, the development of additional good method and soaps, the development of additional good methods seems to be essential.

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PATENT THOUGHTS AND TRENDS

(Continued from page 777)

than by developing these possibilities to the utmost.

(*c*) *Opposition proceedings.*—It has often been suggested that, when a patent is ready for issue, its general nature be made known and the submission of references by interested parties invited. It would be expensive to do this, and the Patent Office would need more funds if it were to be introduced as a procedure. But it would most certainly result in very few patents being issued and later found invalid because of prior descriptions in scientific or technical literature. Those in the line of business to which the patent referred would have great incentive to submit references. It would greatly decrease the number of patent applications filed on doubtful matters, merely as a precaution against patents appearing in the hands of competitors. It would undoubtedly save business far more than its total cost. It would do no harm to the individual inventor. There is no more cruel act than to issue to a lone inventor a patent which he trusted as valid, only to find later that he was not the original inventor at all. Of course such a procedure needs to be safeguarded against undue delay; there should be no possibility of argument that would allow a vigorous group to block the application of an individual inventor indefinitely. The submission of references, and brief statements regarding them, should be all that should be allowed. The Office should still adhere to the procedure of maintaining an applicant's material secret until it has formulated a patent ready for issuance to him, and the procedure here suggested should be a final step leading only to one Office action to which the inventor may respond. There is no doubt that it places a burden on industry, but this would be greatly lessened when mechanization of search becomes accomplished. There are numerous pros and cons. But the procedure here suggested, which has been advanced many times, certainly warrants careful examination.

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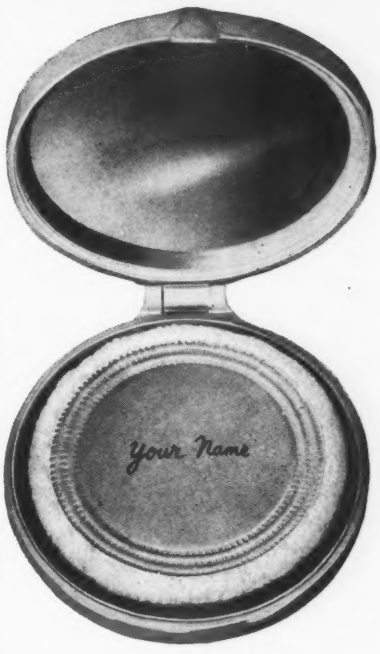

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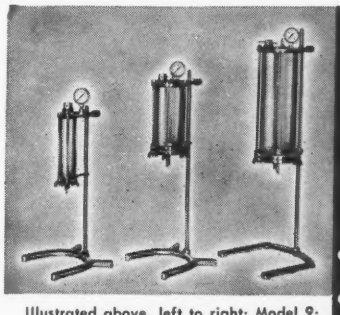

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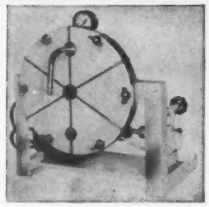

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selves fully versed in special technical fields.[56]

It is recommended, therefore, that technical matters involving patents be determined by a special tribunal set up for the purpose. For example, whenever the validity of an issued patent is challenged before any court, or whenever scientific and technical questions involving the validity, scope, or infringement of issued patents are raised in any court, whether by a declaratory judgment proceeding or otherwise, all such issues and questions should be referred by the courts in which they arise to a special administrative tribunal for findings of fact.

It is recommended that such an administrative tribunal be established within the Department of Commerce. It should be independent of the Patent Office, but should have complete access to the files of that Office pertinent to any cases before it. This should include bringing examiners before it for testimony. Its procedures should be similar to those which have become common for administrative tribunals generally. It should certainly have the authority, and the funds, to call before it and to advise with independent experts in the field, in addition to examining the experts provided by litigants. This tribunal should be staffed, by Presidential appointment, with the most competent men available.

It should be the function of such a tribunal, upon any reference by a court, to give full public notice of hearings on the matters raised by the reference. At such hearings the tribunal should be enabled to receive evidence and argument offered by any interested person, whether or not a party to the action pending before the court. This, however, should not prevent a third party from later raising the same or similar issues in the courts, especially upon the finding of new evidence.

The decisions of this tribunal upon matters referred to it by a court, together with all pertinent findings of fact, should promptly be made available to the referring court. Thereafter, the factual findings by the tribunal should be final and conclusive on all matters in issue, subject to the normal considerations of judicial review of administrative findings. It should be left to the courts to determine whether patents should be invalidated, and to specify relief in cases of infringement. This follows since legal questions, entirely apart from the technical facts involved, will often arise. But the burden on the courts would be greatly reduced, and transferred elsewhere to be handled at less cost and delay.

In this way it should be possible to secure sound, expeditious, and not too costly decisions on patent questions. Moreover, the number of suits filed in more than one court should decline abruptly after this procedure is inaugurated. Similarly the presumptive validity of issued patents should be enormously strengthened.

It is fitting that technical issues of this kind be resolved in a tribunal specially qualified for the purpose.[57] It is also fitting that this tribunal should have the full benefit of the facilities and records of the Patent Office. Moreover, patent litigations usually present issues, facts, and claims which were not before the Patent Office when a patent was originally issued, and it is desirable that a tribunal close to the Patent Office have an opportunity to review issued patents in the light of these newly presented issues, facts, and claims. This is particularly so, since very frequently the issues, facts, and claims which are subsequently raised in litigation before the courts would have precluded the original issuance of the patent had they been raised at the time in the Patent Office.[58]

3. The misuse of patents, so as to perpetuate patent monopolies through combinations, cross-licensing and improvement patents, should be remedied

Exchange of licenses among patent owners is in general desirable. Limited monopoly for the statutory period by a single industrial unit, based on its own original patents together with such licenses from others as will enable it to operate, is also desirable. The situation to be prevented is one where, through patent interchange and the retention by the interchanging group of exclusive operating rights under patents, a combination of industrial units dominates a given field of commerce, excluding newcomers therefrom. This situation becomes even more undesirable when it is perpetuated by continuing accretions to its patent structure. This cannot be controlled to maximum public advantage under the Antitrust Acts, for they were not designed with this specialized problem especially in mind. The doctrine of misuse, which bars relief to the plaintiff in infringement suits, often connected with antitrust violation, has resulted in destruction of patents in cases where other action could be more beneficial to the patent system as a whole. We should have a sound patent system, and then the destruction of the patent grant should be earnestly avoided. Legislative guidance as to remedies would greatly aid the courts in this matter.

Similarly, although continued improvement of products and processes is most essential, patents on improvements should not be a means of perpetuating the original and limited monopoly afforded by an earlier patent. While it is in the public interest that full patent protection should be given to a basic invention in order that venture capital may be attracted to its support, the perpetuation of that patent monopoly is often not necessary to bring improvements on that invention into use for the public benefit. In particular, if there is no serious competition in the field of commerce covered by a patent, the introduction, by the owner of the patent, of an improvement into use in that field does not depend upon the extension of a patent monopoly to the improvement. In such a situation, it is normally sufficient if the patent owner is assured of a return in the form of reasonable royalties from general licensing. In a situation, however, where the field of commerce covered by a patent is highly competitive the extension to the owner of the patent of a temporary patent

monopoly with regard to improvements may still be necessary in order to attract the venture capital needed both for research on improvements and for the introduction of improvements into use.

To prevent the perpetuation of business monopolies through the use of patents on improvements, accordingly, a remedy should be devised. Such a remedy should draw a distinction, however, between a competitive situation, where the earnest search for improvements becomes a feature of the competition, and the situation where basic patents give unitary control over the art, and patents on improvements merely perpetuate that control. In the former case, the protection of a temporary patent monopoly for the improvement is essential. (To be Continued)

REFERENCES

[53]See op. cit., supra, footnote **50.** Also Progress of Researchin Machine Searching for the Patent Office, by Jenney, American Patent Law Association Bulletin, March **1956,** pp. **123-125.**

[54]See table submitted by P. J. Federico, Examiner in Chief, Patent Office, Washington, D.C., in U.S. Congress, Subcommittee on Patents, Trademarks, and Copyrights, of the Senate Committee on the Judiciary, American Patent System, hearings, October **10-12, 1955,** pp. **291-293.**

[55]See article by Jenney in footnote **53,** supra.

[56]See report and bibliography on a Single Court of Patent Appeals being prepared by the American Law Division, Legislative Reference Service, Library of Congress, for the Subcommittee on Patents, Trademarks, and Copyrights of the Senate Committee on the Judiciary.

See also footnote **51,** supra, and Judge Frank's concurring opinion in *Picard* v. *United Aircraft Corporation,* **128** F. 2d **632,** at **639-640** (2d Cir. **1942**).

[57]Invention and Public Policy, by Stedman, Law and Contemporary Problems, vol. **12,** autumn **1947,** pp. **649-679,** especially p. **659** and references cited on that page.

[58]See footnote **54,** supra.

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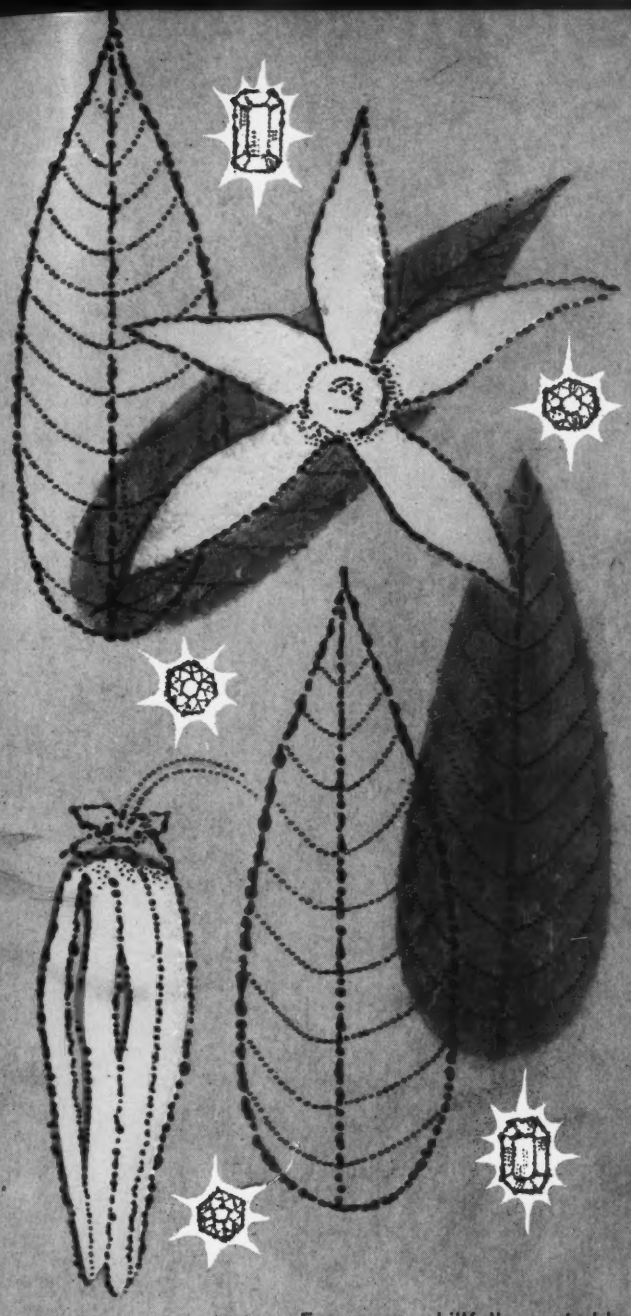

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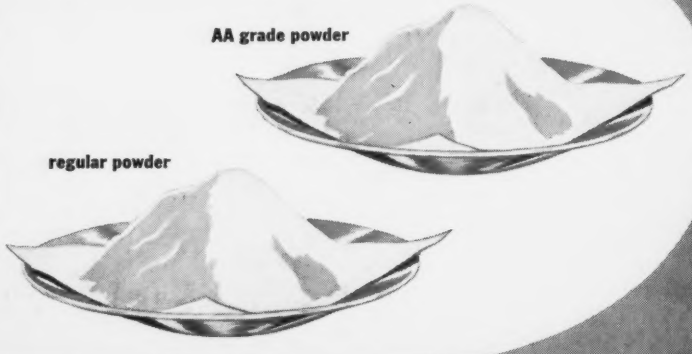

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Branch Offices: Chicago, Ill.; San Francisco, Calif.; Vernon, Calif.; Atlanta, Ga.; Dallas, Texas